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STUDIES IN HODGKIN'S SYNDROME

I. A DISTRIBUTION STUDY OF HODGKIN'S DISEASE IN THE UNITED STATES

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With the Technical Assistance of
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Although much has been said about the part played by many infectious agents in the etiology of the disease entity described by Thomas Hodgkin[3] in 1832, no satisfactory statistical surveys have appeared relative to its comparative distribution in communities, states, and countries; in rural and urban populations; and in different races and climates. Information relative to the geographic and racial distribution of disease has become of increasing importance to the American physician as he himself has become migratory or as his patients may now come to him from a sojourn anywhere in the world. The possible nature of the as yet undetermined etiology of certain well established disease syndromes may be suggested by such surveys, and for this reason the present analysis was begun some two years ago as a part of an intensive study of the very considerable range of clinical and pathologic states grouped under the general designation of Hodgkin's disease. It must be said, however, that just as Thomas Hodgkin in his original report presented a series of cases, which were later recognized by careful microscopic study to comprise lymph node pathology of divergent underlying etiologies, so we, at the present time, are not certain that all of the histopathological abnormalities grouped under the heading of Hodgkin's syndrome are necessarily due to the same etiologic agent. A classification and re-emphasis of the range of clinical and histological findings observed in Hodgkin's disease has recently been presented by Jackson and Parker.[4] It is interesting to note that, just as in similar previous analyses by other workers, there is again noted a very wide variation in both clinical and histopathological patterns grouped under the general term Hodgkin's disease; from a relatively benign "infectious" granuloma on the one hand to an invariably fatal sarcoma on the other.

The presence in Hodgkin's tissue of mycobacteria, diphtheroids, amoebae, fungi, common bacterial invaders of the upper respiratory tract, small, gram-positive, anaerobic, gas-forming rods, Brucella, and viruses has been reported in the literature. Most of the infectious agents isolated have been subsequently

[1]Hodgkin's disease research carried on in the Division of Research, Department of Medicine, Ohio State University, is made possible in part by the Elise S. L'Esperance Fellowship Fund and by the Comley Research Fund.

[2]The maps representing the incidence of avian tuberculosis and Bang's disease in cattle are printed with the consent of the U. S. Department of Agriculture.

[3]Hodgkin, Thomas. "On Some Morbid Appearances of the Absorbent Glands and Spleen." Tr. Roy. Med. Chir. Soc., Vol. 17, 1832, pp. 68–114.

[4]Jackson, H., Jr. and Parker, F. Jr. New Eng. Journ. of Med., Vol. 230, No. 1, Jan., '44, pp. 1–8.

discarded as etiologic factors because of their failure to produce the clinical and histopathological picture of Hodgkin's disease in experimental animals, and because of conflicting and irreconcilable reports from diverse sources. Due, however, to the nature and chronicty of the clinical course, the location and granulomatous character of the lesions, and the actual demonstration of acid fast organisms in some cases, the tubercle bacillis has remained under suspicion since Sternberg's first report[5] and has been the subject of many subsequent investigations. A few among those who have adduced direct or circumstantial evidence as to its possible causal relationship to Hodgkin's disease are Sternberg,[5] Lichtenstein,[6] Fraenkel and Much,[7] L'Esperance,[8] and Stewart and Doan.[9] On the other hand, van Rooyan,[10] Twort,[11] Branch,[12] Reed,[13] Longcope,[14] Terplan and Mittelbach,[15] Uddstromer,[16] Jackson and Parker,[4] and others have expressed their unwillingness to accept this etiologic relationship. Classical tuberculous lesions have been demonstrated at post mortem in association with lesions typical of Hodgkin's disease in about twenty to thirty per cent of deaths attributed to the latter. When one considers conversely, however, the incidence of Hodgkin's disease in patients with proven clinical tuberculosis the correlation is found to be much lower. Medler is reported by Jackson and Parker[4] to have found that only 0.3 per cent of a large series of tuberculous patients examined at autopsy showed the histopathological changes of Hodgkin's disease; and Uddstromer[16] has reported that in Sweden the occurrence of Hodgkin's granuloma in areas where the incidence of tuberculosis is high, was actually less than in areas where the latter was low.

The suggestion made by L'Esperance that Hodgkin's syndrome may be caused by an avian tubercle bacillus[8] or an atypical mycobacterium[17] of hitherto unrecognized pathogenic importance renders a comparison of human tuberculosis with Hodgkin's disease of less significance, since the incidence of atypical infections due to strain of acid fast bacilli other than human and bovine pathogens does not follow or parallel the incidence of human pulmonary tuberculosis.

Parsons and Poston[18] and Forbus[19] have recently reported the isolation of organisms of the Brucella group from patients with typical Hodgkin's lesions, but no convincing confirmation of their very interesting and suggestive observations has as yet been published.

The incidence of Hodgkin's disease among all post mortem examinations done at general hospitals is given by Symmers[20] as 0.16%; Barron,[21] 0.32%; Ciechanowski,[22] 0.33%; and Jackson and Parker,[4] 0.25%.

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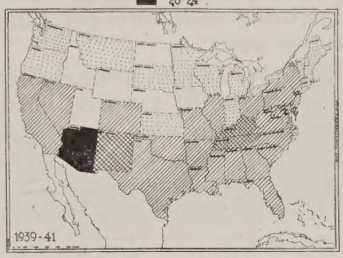
[5]Sternberg, C. Ztschr. f. Heilk 19: 21, 1898.
[6]Lichtenstein, A. Frankfurt Ztschr. f. Path. 24: 29, 1921.
[7]Fraenkel, E., and Much, H. Ztschr. f. Hug. u. Infekt. 67: 159–200, 1910; 99: 391, 1923.
[8]L'Esperance, E. S. J. Immunol. 16: 27–36, Jan., 1929; 16: 37–60, Jan., 1929.
[9]Stewart, F. W., and Doan, C. A. Annals of Surg., p. 141–52, 1931.
[10]van Rooyen, C. E. Brit. Med. Jour. 1: 50–51, Jan. 14, 1933.
[11]Twort, C. C. Journal Path. and Bact., Vol. 33: 539–546, July, 1930.
[12]Branch, A. Arch. Path. 12: 253–274, August, 1931.
[13]Reed, D. M. J. H. H. Rep. 10: 133, 1902.
[14]Longcope, W. T. Bull. Ayer Clin. Lab. Penn. Hosp. 1:1, 1903.
[15]Terplan, K., and Mittelbach, M. Virchows Arch. f. Path. Anat. 271: 759–866, 1929.
[16]Uddstromer, M. Acta. Tuberc. Scandinav., supp. 1, pp. 1–225, 1934.
[17]L'Esperance, E. S. Personal Communication.
[18]Parsons, P. B., and Poston, N. A. South Med. Jour. 32: 7–13, Jan., 1939.
[19]Forbus, W. D., and Gunter, J. U. South Med. Jour. 34: 376, 1941.
Forbus, W. D. Am. J. Path., Vol. 18, No. 4, July, 1942.
[20]Symmers, D. Arch. Int. Med. 4: 218, 1909; Arch. Int. Med. 21:237, Feb., 1918; Am. J. Med. Sci. 167: 313–339, March, 1924; Am. J. Med. Sc. 174: 9–29, July, 1927.
[21]Barron, M. Arch. Path and Lab. Med. 2: 659–690, Nov., 1926; J. A. M. A. 87: 1445, 1926.
[22]Ciechanowski, S. Virchows Arch. f. Path. Anat. 303: 206–222, 1938.

DISEASES OF THE HEART (90-95)
1941
125-185
185-245
245-305
305-365
365-425

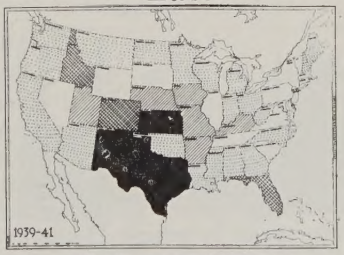
HODGKINS DISEASE MORTALITY
1939-41
.4-.8
.8-1.2
12-16
16-20
20-24

DIABETES MELLITUS (81)
1939-41
5-12
12-19
19-26
26-33
33-40

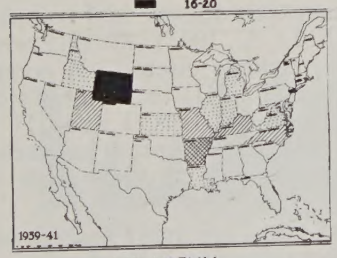


TUBERCULOSIS CASE MORTALITY
10-20 per 100,000
20-40
40-60
60-80
80-100+

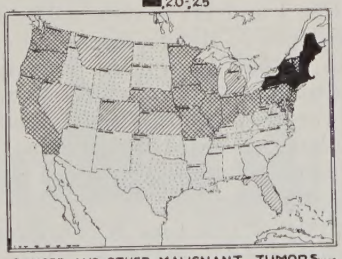
CIRRHOSIS OF THE LIVER (126)
1939-41
0-4
4-8
8-12
12-16
16-20



BRUCELLOSIS CASE MORTALITY
.00-.05 per 100,000
.05-.10
.10-.15
.15-.20
.20-.25



TULAREMIA
MORTALITY PER 100,000
.000-.025
.025-.050
.050-.075
.075-1.00
1.00-1.25+



CANCER AND OTHER MALIGNANT TUMORS (44-59)
1941
50-75
75-100
100-125
125-150
150-175

METHODS

All the data concerning mortality between the years 1939 and 1941 presented in the accompanying charts (Plates I and II) were furnished by Dr. Halbert L. Dunn, Chief Statistician for Vital Statistics, Bureau of Census, Washington, D. C. No data previous to the year 1939 were used because of the revision in the International List of Causes of Death in respect to Hodgkin's Disease during the preceding year. "In 1938 the International List was revised and, effective in 1939 and thereafter, the conditions accepted for tabulation as Hodgkin's Disease were narrowed down to include only Hodgkin's Disease, Lymphatic Anemia, Lymphogranuloma, Lymphogranulomatosis, Pseudoleukemia (only when mentioned in connection with Hodgkin's disease)."[23]

Statistics concerning the incidence of brucellosis and avian tuberculosis in animals (Pl. III) were obtained from the U. S. Department of Agriculture. The data representing mortality per hundred thousand in each disease entity were treated in two ways:

1. Maps (Pl. I) were compiled showing distribution by means of five gradations of the degree of positive incidence, represented by pure white, stippled, single cross hatch, double cross hatch, and solid black in order of increasing magnitude.

2. Another series of companion charts (Pl. II) were compiled using bars of forty-nine lengths to represent the relative order of magnitude of each state among its sister states and the District of Columbia. All states with a zero mortality in a given map are represented as first in order of increasing frequency. Similar statistics for heart disease, diabetes, cirrhosis of the liver, cancer, and other malignant tumors, and tularemia were selected for comparison and contrast.

RESULTS

A consideration of the data available for Hodgkin's disease (Pls. I and II) reveals that its greatest reported mortality is in the state of Maine. The coastal and north central states show a rather high mortality, the actual number of cases reported in the northern half of the United States being almost twice that observed in the southern half. The distribution of human tuberculosis (Pls. I and II) is entirely dissimilar; in fact, the general areas in which tuberculosis mortality is greatest are areas in which Hodgkin's disease is reported least often. The distribution of avian tuberculosis in fowl (U. S. D. A., 1931) (Pl. III) seems to be only remotely similar to Hodgkin's disease. A map issued by the U. S. D. A. in 1941 (Pl. III) is even less suggestive. The distribution of brucellosis mortality in man (Pls. I and II) is very unlike that of Hodgkin's disease; and consideration of the incidence of Bang's disease in cattle (U. S. D. A., 1941) (Pl. III) reveals no parallel to human brucellosis mortality or to Hodgkin's disease. A comparison of the population ratio of white versus other races (Pl. III) to Hodgkin's disease, diabetes, mellitus, heart disease, and neoplastic disease (Pls. I and II) reveals some similarity. The control maps, with the possible exception of cirrhosis of the liver and tularemia, bear an apparent resemblance to themselves and to Hodgkin's disease.

In a study of this type it is appreciated that there are many sources of error. A few of these may be stated as follows: differences in economic level; in population ratio of white versus other races; in medical acumen, in opinion as to diagnostic criteria, in availability of diagnostic facilities, and in migration across state borders.

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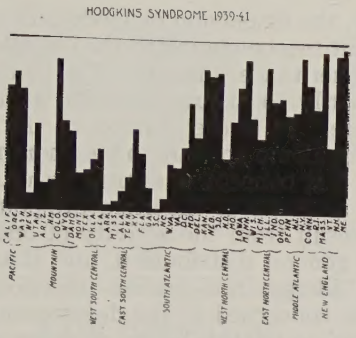
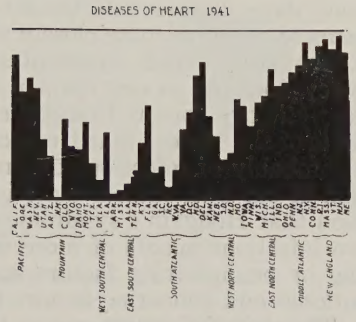
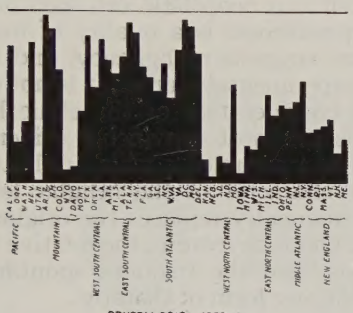
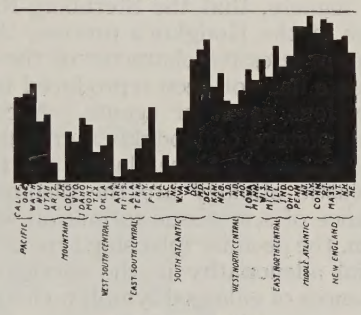
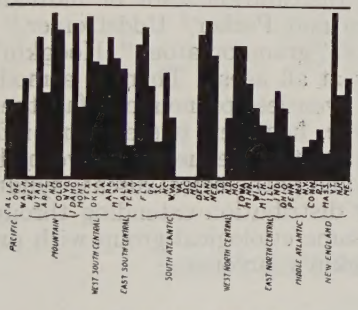
[23]Dunn, Halbert L. Personal Communication.

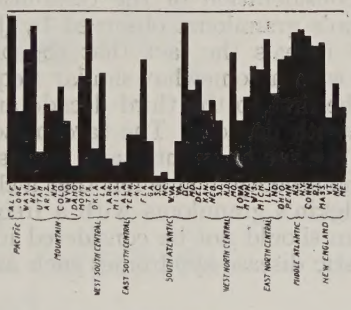

HODGKINS SYNDROME 1939-41

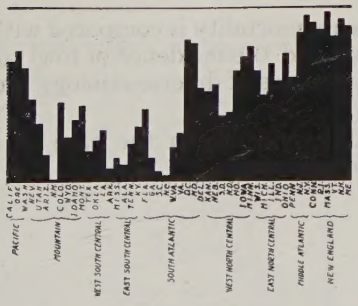

DISEASES OF HEART 1941

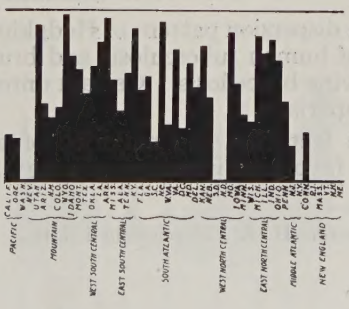

TUBERCULOSIS 1939-41


DIABETES MILLITUS 1939-41


BRUCELLOSIS 1939-41


CIRRHOSIS OF LIVER 1939-41


CANCER & OTHER MALIGNANT TUMORS 1941


TULAREMIA 1939-41

DISCUSSION

Among those diseases selected for study, the dispersion of Hodgkin's mortality data seems to resemble more closely those entities belonging to the so-called degenerative, metabolic, and constitutional inheritance groups. The inclusion of malignancy does not in our opinion necessarily constitute evidence in favor of a neoplastic etiology for all Hodgkin's disease. It is the opinion of the majority of students of the subject that Hodgkin's granuloma appears to be a non-malignant process, probably of infectious origin, and this concept is shared by us. A consideration of our own clinical material and a review of the literature points to the suggestion that Hodgkin's syndrome may result from the activity of one or more co-active infectious agents of more or less general distribution, and that definite localizing or precipitating factors such as allergy, non-specific infection, injury, constitutional and endocrine factors may be concerned in the development of the lesion. The claim for malignancy in Hodgkin's syndrome hinges on many equivocal points, namely, that the Sternberg-Reed cell is a neoplastic cell seen only in the presence of the Hodgkin's process, that invasiveness is a quality of malignancy, that the progressive character of the disease suggests malignancy, and that since the disease has not been reproduced in an experimental animal, it is not caused by an infectious agent or agents. A careful consideration of the clinical and histological picture of Hodgkin's granuloma is the most convincing evidence of the tenuous nature of these claims. A few of the arguments which militate against a neoplastic etiology are the pleomorphic character of the cellular lesions, the abundance of scar tissue formation which frequently replaces the original cellular reaction, the peculiar relapsing type of fever and tachycardia, the relative frequency of initial adenopathy in the cervical region, and the frequent spontaneous disappearances of enlarged lymph nodes without any form of therapy.

A consideration of the combined age distribution data of individuals with Hodgkin's granuloma observed by Jackson and Parker,[4] Uddstromer,[14] and ourselves[24] reveals the fact that the onset of "granulomatous" Hodgkin's disease occurs with a somewhat similar frequency at all ages. There is a moderate rise from the first to the third decade and an even less pronounced fall thereafter to the seventh decade. The sarcomatous type, however, is seen very infrequently before the age of twenty, and occurs with greatest frequency between the ages of fifty and seventy. It is felt that a clinical and pathological disease syndrome such as Hodgkin's granuloma with a frequency distribution extending throughout the life span should not be considered in the same etiological group with presumably neoplastic disease syndromes such as Hodgkin's sarcoma.

SUMMARY AND CONCLUSION

The dispersion pattern of Hodgkin's disease mortality is compared with the mortality of human tuberculosis and brucellosis and the incidence of fowl tuberculosis and bovine brucellosis. Certain unrelated diseases of diverse etiology are reviewed for comparison.

The fact that the majority of available evidence in the case of Hodgkin's disease favors an infectious etiology is re-emphasized.

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[24]Hoster, H. A. Unpublished data.

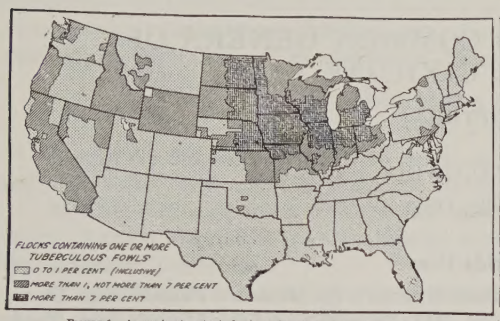

FLOCKS CONTAINING ONE OR MORE TUBERCULOUS FOWLS
0 TO 1 PER CENT (INCLUSIVE)
MORE THAN 1, NOT MORE THAN 7 PER CENT
MORE THAN 7 PER CENT

FIGURE 1.—Approximate extent of avian tuberculosis in the United States.

AVIAN TUBERCULOSIS
1931

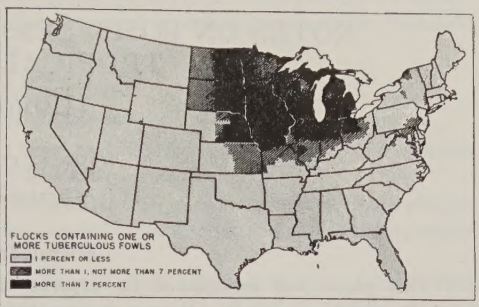


FIGURE 3.—Approximate extent of avian tuberculosis in the United States on January 1, 1941.

AVIAN TUBERCULOSIS

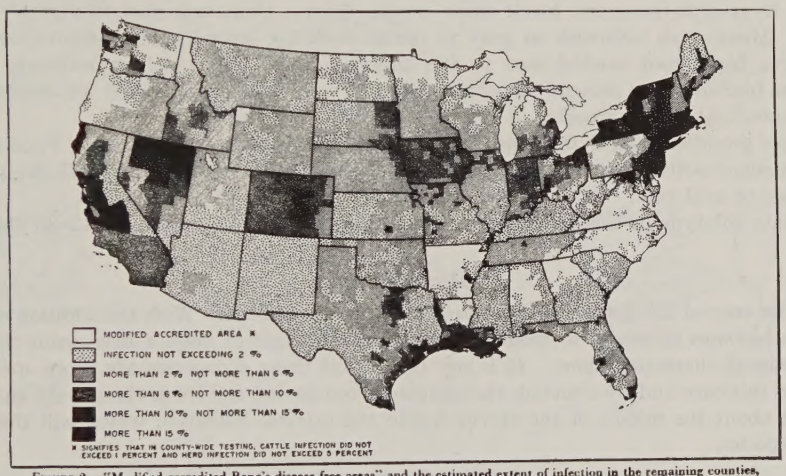
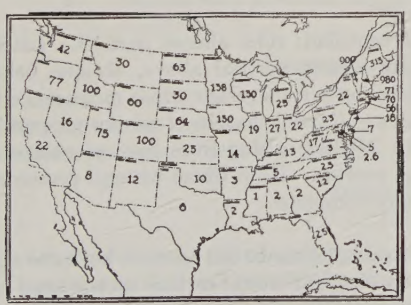
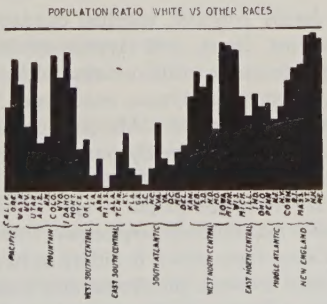

MODIFIED ACCREDITED AREA *
INFECTION NOT EXCEEDING 2 %
MORE THAN 2 % NOT MORE THAN 6 %
MORE THAN 6 % NOT MORE THAN 10 %
MORE THAN 10 % NOT MORE THAN 15 %
MORE THAN 15 %
* SIGNIFIES THAT IN COUNTY-WIDE TESTING, CATTLE INFECTION DID NOT EXCEED 1 PERCENT AND HERD INFECTION DID NOT EXCEED 5 PERCENT

FIGURE 2.—"Modified accredited Bang's disease-free areas" and the estimated extent of infection in the remaining counties, November 1, 1941.

BANGS DISEASE IN CATTLE, 1941
(Brucellosis)



POPULATION RATIO
WHITE — OTHER RACES



NOTES ON SOME LESS COMMON GENERA OF TROPICAL CIXIIDAE

(HOMOPTERA)

JOHN S. CALDWELL,
Circleville, Ohio

Microledrida Fowler

This genus was established for *asperata* from Guerrero in Mexico. *Fuscata* Van Duzee from California occurs in adjacent Sonora (M. F. 209, Dampf) and *fulva* Metcalf from Texas has been taken in Tamaulipas (Caldwell).

Microledrida virida n. sp.

Length 5 mm. Vertex green with three red incomplete transverse stripes; extreme apex yellow. Eyes with transverse black stripe across center. Pronotum next to vertex red; green caudad. Mesonotum yellowish to gray in center with the lateral compartments fuscous and including a black spot caudad next to the lateral carinae. Elytra clear; infuscate basad; a transverse fuscous stripe present across furcations of main veins; each apical cell with a diffused fuscous spot. Abdomen greenish.

Vertex produced, longer than mesonotum, with prominent median carina. Face extremely flat; no median carina present. Sutural margin of elytra with vertical thin plate-like projection at junction of anal vein.

Female holotype of this large species from Peten Lake, Guatemala, 11–12–25 (M. F. 734. Dampf).

Micrixia Fowler

Fowler erected this genus for the unique *costalis* from Mexico. With the addition of another species it becomes necessary to modify the original definition or erect a new genus that differs by veinational characters alone. It is my belief that these characters are more specific than generic in this case and by omitting the statement concerning the freak claval vein entering the suture at about the middle of the clavus accept the original definition which will then include the two species.

Micrixia nigra n. sp.

Length 3.2 mm. Black over all with carinae of vertex, all of pronotum, and legs smoky. Face not as narrowed as in *costalis*. Elytra with normal claval veins; medius not branched; two apical cells formed by medius and adjacent veins very long; only two subapical cells present, these formed by cubital and radial veins.

Female holotype from three miles north of Acapulco, Guerrero, 11–22–38 (Caldwell).

Diastrocixius n. gen.

Vertex deeply concave, notched caudad, carinate cephalad; sides almost parallel. Lateral carinae of vertex, frons, and clypeus greatly elevated, almost vertical above, oblique below. Frons widened to apex; median carina forked basad forming a transverse carina; median ocellus prominent. Carinae of clypeus evanescent toward apex. Caudal margin of pronotum parallel to caudal margin of vertex. Mesonotum tricarinate. Medius arising from base of subcostal-radial stock. Veins indistinctly punctate; stigma long, narrow. Hind tibiae without prominent spurs. Pygofers of female robust; ovipositor seemingly complete.

Type: *Diastrocixius thelyus* n. sp.

This genus resembles *Bothriocerodes* Fowler in general appearance but in most keys the male will run to *Cixius* from which it differs in having greatly elevated lateral carinae on the head and the two carinae between the crown and forehead are widely separated and not connected by a median carina. Fowler does not mention or show a double carinae on the forehead and in his

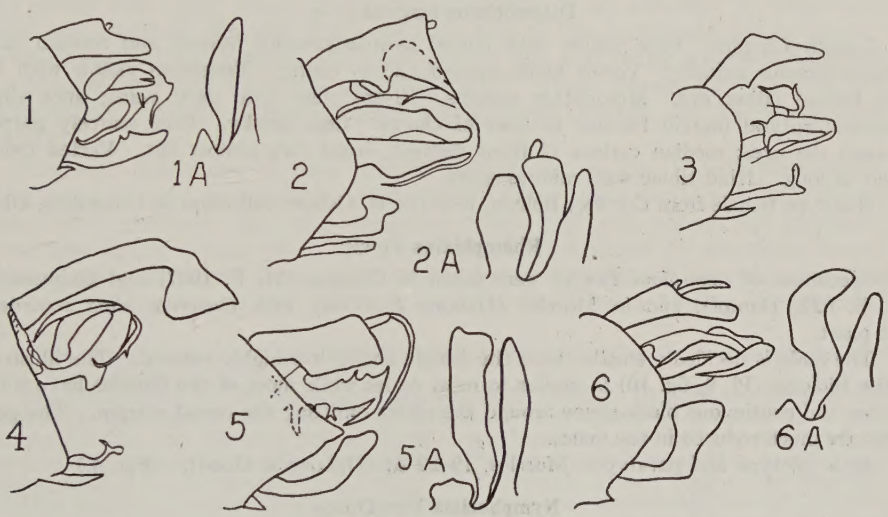
illustrations the lateral carinae are not as elevated as in the species before me; therefore I believe *Diastrocixius* is distinct from *Bothriocerodes*. Its true placement is probably in the tribe *Pintaliini* although the elytra are not as steep as in *Pintalia*.

Diastrocixius thelyus n. sp.
(Figs. 1 and 1-A)

Length 6.5–7.5 mm. Eyes black, ocelli red; head and thorax yellow; abdomen sometimes red; legs yellow with apical tarsi smoky; elytra clear with yellow veins.

Median carina of frons short, visible only in basal third. Anal segment of male simple, short. Lateral margins of pygofers broadly obtuse caudad; medio-ventral process short, acute. Styles slender, lanceolate.

Male holotype, female holotype, and paratypes from Vergel, Chiapas, May and June, 1935 (M. F. 4268, 4253 and 4239), male paratype, Elzapote, Chiapas, 9–12–30 (M. F. 1821), and fifty female paratypes, Esmeralda, Chiapas, 11–18–30 (M. F. 1934 and 1937) (Dampf).



1. *Diastrocixius thelyus*. Profile of male genitalia.
1-A. Ventral aspect of right forcep and right central portion of male pygofer.
2. *Diastrocixius aurelus*. Same as 1.
2-A. Same as 1-A.
3. *Nymphocixia vanduzeei* Muir. Same as 1.
4. *Rhamphixius championi* Fowler. Same as 1.
5. *Diastrocixius apicatus*. Same as 1.
5-A. Same as 2-A.
6. *Pachyntheisa concinna* var. *striata*. Same as 1.
6-A. Same as 1-A.

Diastrocixius thelyus var. **basalis** n. var.

Length 8 mm. Color as in *thelyus thelyus* except base of elytra fuscous with this color continuing caudad between claval vein and sutural margin.

Holotype female from Finca Belem, Chiapas, 3–2–38, (M. F. 6497, Dampf).

Diastrocixius aurelus n. sp.
(Figs. 2 and 2-A)

Length 6.5 mm. Head and body yellow, elytra clear with yellow veins. Median carina of frons visible in basal two-thirds; basal fork acute.

Anal segment of male with subapical projection on ventral margins; right margin cut away before apex. Lateral margins of pygofers broadly rounded caudad; medio-ventral process extremely large, as long as styles, pyriform.

Male holotype from Bartica, British Guiana, 4–27–01 (Parish), in Osborn collection at Columbus, Ohio.

Diastrocixius apicatus n. sp.
(Figs. 5 and 5-A)

Length 6 mm. Vertex and thoracic dorsum orange; abdomen black above, venter yellow. Elytra mostly clear; stigmal spot dark with color extending up onto the disc; smoky band present subapically. Under wing with fuscous apex. Entire face narrow; frons not especially widened apically; median carina interrupted only by median ocellus. Anal segment of male constricted basad. Pygofers greatly produced caudad into acute flaps; medio-ventral process short, very broad. Styles large, long; sides roughly parallel. Aedeagus appears to have periandrium separated from penis except basad.

Holotype male, allotype female, and one male paratype from Coroica, Bolivia, in the H. Osborn collection at Columbus, Ohio; one male paratype in writer's collection.

Diastrocixius magnus n. sp.

Length 7.5 mm. Face yellow with lateral carinae broadly fuscous and median carinae of frons fuscous apically. Vertex black caudad and in center. Pronotum yellow with black dash behind either eye. Mesonotum fuscous. Elytra clear with dark veins; apex slightly infuscate; sutural margin fuscous to apex of clavus. Legs smoky. Face scarcely narrowed between the eyes; median carinae of frons distinct; basal fork almost flat. Vertex twice as broad as long. Hind tibiae with minute spurs.

Holotype female from Coroico, Bolivia, is in the H. Osborn collection at Columbus, Ohio.

Rhamphixius Fowler

Specimens of *championi* Fowler were taken in Chiapas (M. F. 1937) and Quintana Roo (M. F. 622, Dampf), and in Morelos (DeLong & Good) with *Crescenta alata* recorded as host plant.

The male is decidedly smaller than the female and is less highly colored. The illustration in the Biologia (Pl. 9, fig. 10) is similar to most males while most of the females have a much heavier and continuous black stripe around the elytra omitting the costal margin. The genital styles are much reduced in the males.

Male allotype and paratypes, Morelos, 19–22–41 (DeLong & Good). (Fig. 4.)

Nymphocixia Van Duzee

Ten specimens were collected in the Canal Zone, Panama, May, 1927, by H. Osborn. The coloration of these specimens is close to *unipunctata* Van Duzee in that the elytra are hyaline and fuscous with a fuscous V across the transverse veins. The male genitalia coincides with the description of *vanduzeei* Muir. (Fig. 3.)

Nymphocixia vanduzeei var. **floridensis** n. var.

Length 6 mm. Very heavily marked. Elytra mostly fuscous with a milky area extending from the commissural margin across to the stigma where it projects basad forming a somewhat broad V-shaped design. This specimen is larger and darker than *unipunctata* or *vanduzeei vanduzeei*.

Female holotype from Manatee Co., Florida, 1–4–25 (T. H. Hubbell), Osborn collection at Columbus, Ohio.

Pachyntheisa concinna var. **striata** n. var.
(Figs. 6 and 6-A)

Length 4–4.5 mm. The central semitransparent band is not interrupted in the middle of each elytra otherwise the color and marking are identical with *concinna concinna* Fowler. The male styles differ in appearance from those shown by Fowler (Pl. IV, fig. 3c), but this may be due to point of view or differences resulting from treatment with caustic.

Male holotype and female allotype from Tenancingo, Mexico, 10–22–33 (Plummer), paratypes from Mexico, D. F., 11–1–39 (DeLong).

THE HISTORY OF OHIO'S NORTHERNMOST COAL MINE

MYRON T. STURGEON,[1]
Michigan State Normal College,
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The Zeil Pfouts farm, located 2.7 miles northwest of Burton Village in Geauga County, Ohio, is similar in appearance to many of the well kept farms in that vicinity. The Pfouts farm, however, has one distinction that is shared with no other farm in the vicinity for miles around; for between 40 and 60 years ago coal was mined from beneath its acres. This mine was unique in that it was the farthest north of any coal mine ever operated in Ohio. (See Figure 1.) The only other near coal mines, with the exception of an attempt to mine coal 2.15 miles southwest of Welshfield on the east side of the Cuyahoga River, are at least 15 miles farther south along the north-south line and being somewhat farther east or west are actually 25 or 30 miles distant.[2] These mines are in the vicinity of Tallmadge in Summit County, Palmyra in Portage County, and Vienna in Trumbull County.

Concrete evidences of past mining operations on the Pfouts farm have long since been almost completely obliterated. The mine buildings and equipment have been removed, the mine openings filled, and cultivated and pasture fields cover the former mine sites. A green meadow without an apparent trace of a mine opening or mine dump now extends over the site of the main shaft which was located approximately 100 feet west of the Pfouts house. Only small bits

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[1]This historical account was written at the suggestion and with encouragement of Wilber Stout, State Geologist of Ohio.

The compilation of the historical data was made possible through the help of numerous persons in the Burton and nearby communities. The following persons have furnished information: Charles Burnett, Frank Davis, Lynn Mumford and nephew, Ben Owen, David Owen, Miss Margaret Owen, Zeil Pfouts, R. R. Phillips, Frank Taylor, Mrs. Ina Taylor, F. H. Thwing, and J. M. Zethmayr. J. J. Feicht, of Cleveland, gave a copy of the original lease, and Miss Annie Ashton, of Chardon, copied lease records at the Geauga County Courthouse.

Special acknowledgment is due Miss Bertha Buell and James Glasgow, who read and criticised the manuscript, J. R. Hickman, who aided in the preparation of the photographs, and Miss Anne Frankenberry, who did the typing.

[2]On November 26, 1943, I made an attempt to find the location of the coal prospect near Welshfield in Troy Township, Geauga County. Mr. Frank Taylor kindly directed me to the site, but in the limited time available I was unable to find any positive surface evidence of the attempted mining. The following are published references to this unsuccessful coal mine:

"In Troy township, the Coal-measure sandstone is separated from the Conglomerate by the coal shales, which are, in places, very thin, and rarely exceed a thickness of six feet. In the southern part of the township, coal has been obtained in small quantities from a seam too thin to be profitably worked. Yet at this point it is probably thicker than in any other part of the county on the east side of the Cuyahoga."—Read, M. C., "Sketch of the Geology of Geauga County," *Report of Progress of the Geological Survey in 1870*, p. 466, Geol. Surv. Ohio (1871) and Read, M. C., "Geology of Geauga County," Geol. Surv. Ohio, Vol. I, Pt. I, p. 521 (1873).

"Evidences of the existence of coal were discovered in 1848–9 on land located in section sixteen, then belonging to Rensselaer Smith, now to Peter Davis. Jehu Brainard, a noted geologist then living in Cleveland, examined the premises, and decided that coal did not exist there in paying quantities. Mr. Smith was not satisfied with this decision, but went to Pennsylvania and procured a practical miner, to come and develop whatever might be found. A few bushels of coal were taken out, which were used by our blacksmiths, but after prospecting less than one hundred feet, the 'mine' came to an abrupt termination. The cavity is now abundantly supplied with excellent water of a very low temperature."—Chapman, William H., "Troy," *Pioneer and General History of Geauga County, Ohio* (Symposium), p. 623, published by the Historical Society of Geauga County (1880).

of dark shale and coal mixed in the soil betray the former existence of a mine there. Approximately 300 feet northeast of the Pfouts house is a broad shallow ravine. Near an old beech tree in this ravine was located the oldest mine opening on the farm from which coal was taken. (See Figure 3.) Some 25 feet southeast was another which was probably a secondary one. These two furnish the best surface evidences of mining operations. There is a low pile of weathered shale largely concealed by blackberry bushes and rubbish. A depression and several

FIG. 1. Map of Ohio showing the location of the coal mine near the Village of Burton in Geauga County and the distribution of the Pennsylvanian and Permian Systems (Coal Measures) by stippling.

cave-ins partly filled with rubbish and field stones mark the entrance and the course of the main slope. A depression is all that is indicative of the location of the secondary slope. Within a radius of 400 feet around the house, Mr. Pfouts showed me seven additional locations of mines, two of which were slopes and five of which were shafts. They were used for ventilation, drainage, and removal of coal. This number does not include numerous prospect pits which were dug from time to time both before and during the operation of the mines. The approxi-

mate locations of the ten mine locations are shown in Figure 2. Without Mr. Pfouts' help it would have been impossible to find the locations of most of them; for, as already mentioned, the surface evidences of their sites, consisting of bits of dark shale and coal mixed in the soil, a tiny weathered shale pile, slight depressions, and now and then a fresh cave-in, are meager. When cave-ins occur, they are filled as quickly as possible with whatever debris is at hand. They have occurred along the east-west road near the Pfouts buildings and in the adjacent fields. On one occasion the road gave way over one of the abandoned mine entries with the passage of a truck loaded with brick and cement. On another occasion the ground in a field on the south side of the road caved under one of Mr. Pfouts'

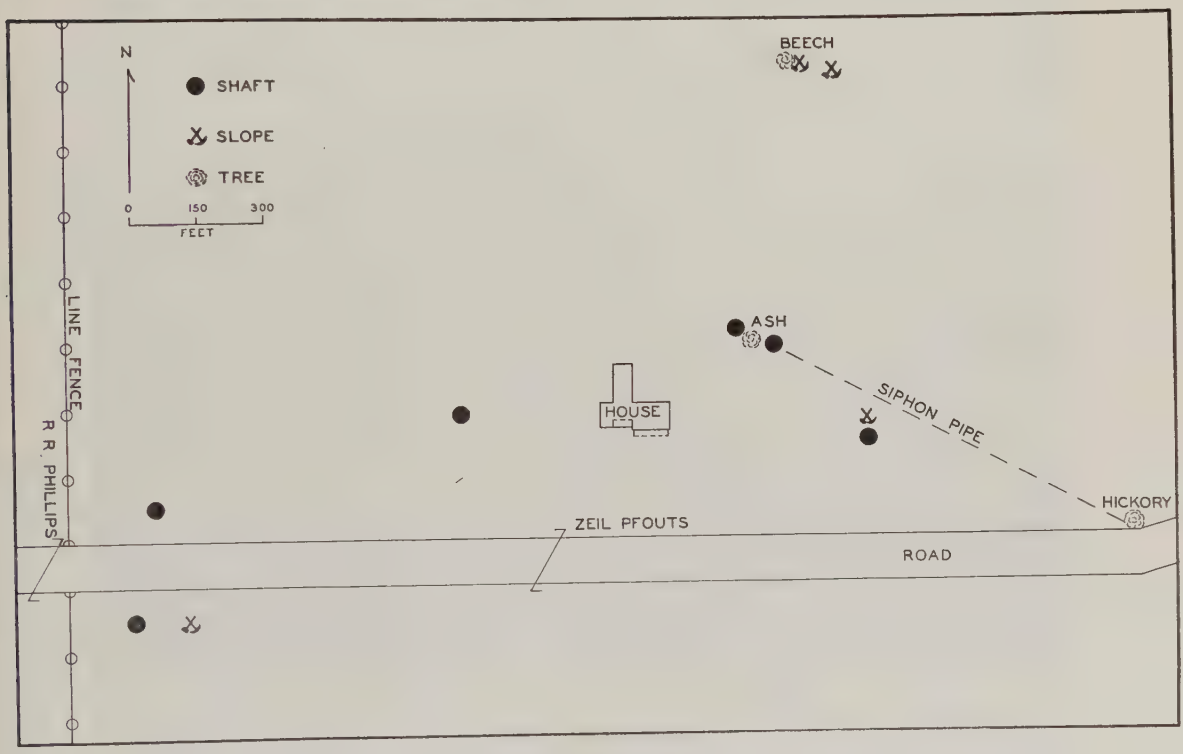

FIG. 2. Map of parts of the Zeil Pfouts and R. R. Phillips farms showing the location of the former mine openings.

horses. With such slight surface indications of mining one could drive past the Pfouts farmstead on the public road for a lifetime and never be aware of the existence of these former mines.

Many of the facts concerning these mining operations have been lost. I have been unable to ascertain how and when coal was discovered in the Burton vicinity. There are no good exposures of coal in the immediate vicinity on account of the almost continuous mantle of glacial till. Nevertheless coal was long ago reported at several nearby places. As early as 1871 Newberry wrote as follows:[3]

> In Geauga county the Briar Hill coal reaches as far north as Burton and Newbury, but only in a narrow strip and detached islands, and is there thin and of little or no value.

[3]Newberry, J. S., "Sketch of the Structure of the Lower Coal Measures in Northeastern Ohio," *Report of Progress of the Geological Survey in 1870*, p. 27, Geol. Surv. Ohio (1871).

In the same report and in a subsequent one published two years later (1873) Read wrote as follows:[4]

> At Burton, the coal shales and the seam of coal are thicker—the rocks of the Coal-measures reaching a thickness of 125 feet; and if the village is to remain without railroads, further exploration of the coal seam, by shafting or drifting, is advisable, as there are indications of coal in sufficient quantities to be profitably mined for local consumption. There is, however, no probability of a supply sufficient to warrant its shipment elsewhere, or to enable the owners to compete, even in the Burton market, with coal from the main coalfields of the State, in the event of a railroad being built. Near the northeast corner of Newberry township, coal of very good quality, about two feet thick, has been disclosed in sinking a well on Mr. Frank Stone's farm, and at a depth of about ten feet from the surface. Here a thin stratum of shale covers the coal, not thick enough to constitute a safe roof; but to the west and northwest, the surface of the land rises, and over a small area it is possible that a sufficient cover may be found to allow of the coal being taken out. The quantity, however, is not large, and what coal there is must be sought near the summit of the hill.

The Frank Stone farm (now R. R. Phillips) lies immediately to the west of the Pfouts farm.

Ford, writing in the *History of Geauga County* published in 1880, makes a brief mention of coal:[5]

> Bituminous coal was found in the hill south of the square, near where George Carlton now lives, by Rev. Dexter Witter and Daniel L. Johnson, esq., but not in paying quantities; and also about three-fourths of a mile north of the "old garden," near the residence of Judge Stone.

No date is given for the discovery by the Rev. Mr. Witter and Mr. Johnson. It is revealed in the above history that the Rev. Mr. Witter first came to Burton in 1821, but did not live there regularly until 1828 and that Mr. Johnson was a boy when his parents moved from New York State to Burton in 1833. Both men were still living when the *History of Geauga County* was written.[6] George Carlton lived in what is now known as Carlton Street on the south edge of Burton. The "old garden" is located at North Burton and is near the Pfouts farm.

Coal is reported to occur on the Lynn Mumford and Frank Davis farms located one mile west and one and three-fourth miles southwest, respectively, of the Pfouts farm.[7] Although coal may once have outcropped on those farms, it is no longer exposed, according to Mr. Mumford and Mr. Davis. Coal is reported by Mr. Mumford at a depth of 43 feet in the drilled well at his milk house. Coal is also reported to have been encountered in other wells drilled in the vicinity, and it is possible that the digging and drilling of water wells played an important part in the discovery of the coal. The wells cited here have been drilled since mining ceased. On the O. Buehner property on the east side of Route 44 and a little less than a mile northwest of the Pfouts farm, two feet of coal are reported at a depth of 42 feet.[8] In the well on the Louis Bukovics property near the west end of Carlton Street in Burton Village, three feet of coal are reported in the interval between a depth of 45 and 60 feet.[9] Only this last autumn (1943) Mr. Burnett reported coal at a depth of 12 feet about one-half mile south of the center at Claridon.

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[4]Read, M. C., op. cit., p. 466 and pp. 521–22.

[5]Ford, W. J., "Burton," *Pioneer and General History of Geauga County, Ohio*, p. 420, published by the Historical Society of Geauga County (1880).

[6]Idem., pp. 485 and 579.

[7]Burnett, Charles, Oral communication, August or September, 1942.

[8]Idem.

[9]Thwing, F. H., Oral communication, September, 1942.

From the available evidence it appears that the presence of coal in the vicinity of Burton was known at least 15 years and possibly much longer before the mining began.

Active prospecting and first mining of the coal on the Pfouts farm began as early as 1884, and prospecting may have been begun even earlier. On May 27, 1884, Edward Blunt and David John leased the coal mining rights from Howard Pfouts, the father of Zeil Pfouts. This lease was assigned to D. E. Owen on May 2, 1891. The June 26, 1884, isues of the *Burton Independent* in a North Newbury news item had the following:

> The coal shaft has been abandoned on account of high water.

FIG. 3. Beech tree and location (at arrow) of the oldest slope northeast of the Pfouts house.

On September 5 of the same year the *Geauga Leader* carried the following in the North Newbury news column:

> After sinking the fifth shaft, coal has been found in paying quantities. Parties from Youngstown are moving their families and are to mine the coal.

A second lease, not identical in wording but very similar in import, is dated June 12, 1885. In it Edward Blunt and David John subleased the coal mining privileges on the Pfouts farm to Edward (Ned) James and M. Owens. On January 1, 1886, the second lease was assigned by Edward James to D. E. Owens, agent for M. Owens.

A copy of the first lease is appended at the end of this account in Appendix I. All of the participants in the leasing of the rights with the exception of Howard Pfouts were Welsh. They came from the Welsh colony at Mineral Ridge, Ohio, with the depletion of the coal in that district. David E. Owens was the husband

of M. (Mary) Owens and the son-in-law of David John.[10] David E. Owen was an accountant, not a miner, but nevertheless it was he to whom the leases were assigned and who directed the mining operations during most of the period of active mining. It seems that David John and Edward Blunt, who had connections with the mining industry in Mineral Ridge, either discovered or learned of the presence of coal on the Pfouts farm and were instrumental in having Mr. Owen assume the leases to coal rights on that property. Although he attempted it, Mr. Owen was never able to lease the coal rights on the George E. Barnes (formerly Frank Stone and now R. R. Phillips) farm, which lies immediately to the west of the Pfouts farm and east of Route 44, although he rented and farmed it and lived there for some time.[11]

The mines were operated under the name of the North Burton Coal Company. The first opening for the commercial removal of coal was the slope by the beech tree northeast of the Pfouts house. Later the main shaft directly west of the Pfouts house was dug, and after a period of mining it too was abandoned. Shortly thereafter other openings were dug along the road west of the Pfouts house and east of the line fence. One of them was a shaft on the north side. A shaft and a slope were located almost directly across the road. The slope, located 40 feet east of the shaft, extended under the road. This is the place where a cave-in occurred under one of Mr. Pfouts' horses a few years ago. The locations of these three mines are only discernible by the bits of dark shale and coal. The slope in the orchard 150 feet due east of the Pfouts house was the last opening from which coal was mined on the farm. Associated with this slope were three lesser shafts. One was directly south of the slope, and two were located northwest near an ash tree. One or more of these shafts may have antedated the slope. They were used for ventilation and for siphoning water from the mine. The only trace of this slope and of these three shafts is an abundance of black shale and coal in the soil. The locations of all of these former mine openings are shown in Figure 2.

Several informants have reported the average thickness of the coal to be 30 to 36 inches and the maximum thickness to be four feet. The coal was apparently deposited in channels or basins and is lenticular in its development. Mineable thicknesses, accordingly, are extremely patchy in distribution. The overburden is thin and probably does not exceed 24 feet in thickness. The following geologic section has been compiled from available sources of information:

5. Glacial till: comprises most of overburden above coal.....15′ to 24′
4. Shale: dark, thin.....
3. Coal: bituminous with some cannel in lower part and with some scattered marcasite throughout, *Sharon*.....2′ 6″ to 3′ 0″
2. Clay: thin, locally present.....
1. "Rock": sandstone or conglomerate, *Sharon*.

Such a roof of till and shale over the coal made mining operations dangerous and troublesome and required timbering for every foot of the underground workings. That greatly increased the labor and costs in mining the coal. Rotting timbers in the old mine openings have permitted the cave-ins from time to time.

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[10]Later in life David E. Owen dropped the "s" from his last name. Herein following the name Owen will be used.

[11]Mr. Owen did not bring his family from Mineral Ridge until 1886, when he with his wife and children moved into the house on the northeastern corner of the crossroad just southeast of Alderman Pond. This house is now in ruins. Later the Owen family moved to the George E. Barnes farm and finally to North Newbury which is at the crossroad west of the Barnes and Pfouts farms. In 1900 Mr. Owen and his family moved to Burton Village.

Water also is reported to have been troublesome. From some openings it was removed by a water cage and from at least one other by a siphon. The siphon pipe extended from a shaft near the ash tree northeast of the house to the bitternut hickory tree at the bend of the road southeast of the house. (See Figure 2.) It was set in operation by means of a pitcher pump. The removal of water from the mine dried up the shallow dug well at the Pfouts buildings.

From the slope by the beech tree the coal was brought out in mine cars hauled by a donkey or a little mule. From the other openings the cars were lifted or pulled by a jenny wheel operated by one or more horses. The jenny wheel and shaft opening were covered by a shed, the sides of which could be removed in warm weather.

The coal contains much sulphur and ash and is only of fair quality. Nevertheless it is reported to have burned well in spite of much ash and many clinkers. The coal is both bituminous and cannel and was used locally for domestic purposes, in the maple sugar camps, and in steam engines. It was sold at the following prices:

Lump coal	$2.50 per ton
Nut coal	2.00 per ton
Slack (used in maple sugar camps)	1.00 per ton

The coal here is the Sharon member or Number 1 coal. It is the oldest coal in the Coal Measures (Pennsylvanian System) in Ohio. This is the same seam that once was extensively mined in northeastern Ohio in the vicinity of Massillon, Mineral Ridge, Youngstown and other communities where it was known as the "Block Coal."

The output of coal from all mining operations on the Pfouts farm was small in spite of the fact that the mines were in operation for almost 20 years. Mr. Owen's record books have been lost or destroyed, and hence it is impossible to determine the total tonnage of coal mined. The mines were idle during the summer months and only one or two miners worked at any time. The equipment and facilities were crude and small in comparison with modern mining equipment. In addition to digging coal, Mr. Owen and his employees did all the necessary blacksmith and carpenter work. They made most of their equipment and tools.

The length of time that any of the mine openings was in operation must have been short. As stated previously, the slope at the beech tree was probably dug in 1884, yet Zeil Pfouts states that this slope and the main shaft west of the house were both already abandoned by about 1890.[12] The last slope in the orchard east of the house was in operation in 1901 and may have continued in operation for one or two years longer.

Not many facts are known about the men who worked in the mines. David John, who was a blacksmith, and Edward Blunt, who is reported to have sold insurance, seem to have been interested in the mining principally as promoters. They probably performed little or no manual labor in prospecting and mining. David E. Owen, however, did all types of work connected with the mine as well as managing it. Edward (Ned) James is reported to have been the first miner

[12]He relates that he was born in 1883 and that he was six or seven years old when the main shaft was filled. An event that happened during the filling of the shaft firmly impressed it on his mind. A team of horses was engaged in hauling debris to fill the shaft. The team was driven too near the open shaft, and the edge caved in and threw one horse over the brink. The weight of the unfortunate horse hanging over the edge and attached to its team-mate by the harness threatened to drag the second horse into the shaft. Quick action in cutting the harness saved the second animal. The other dropped into the shaft, which was partly filled with water, and was drowned.

employed by Mr. Owen and probably did much of the actual work in digging and working the first slope at the beech tree. Later William Bowen, a miner from Mineral Ridge, and Isaac Owen, a half brother of David E. Owen, were employed. They did not like the rural atmosphere of the North Burton neighborhood and remained only a short time. Still later Will Jones, Mr. Owen's nephew, came from Mineral Ridge and worked in the mine for a few months. Mr. Owen's older sons also helped with the mining. Finally there was Christ Maggs, from Girard, Ohio, who helped to dig the slope east of the Pfouts house and who operated it alone until mining was abandoned on the farm.

Although the mining there ended about 40 years ago, interest in the coal has been revived from time to time. The Owen family held the lease to the coal rights on the Pfouts farm for a number of years and made semi-annual payments until August 2, 1922. In 1933, J. J. Feicht of Cleveland leased the Pfouts and Phillips farms and attempted unsuccessfully to strip the coal. Since then James Sober of Salem, Ohio, test drilled the Pfouts and other nearby farms but attempted no mining.

REFERENCES

1. *Report of Progress of the Geological Survey in 1870*, Geol. Surv. Ohio, Columbus, Ohio, 1871.
2. *Report of the Geological Survey of Ohio, Geology*, Vol. I, Part I, Geol. Surv. Ohio, Columbus, Ohio, 1873.
3. *Pioneer and General History of Geauga County*, Hist. Soc. Geauga County, Burton, Ohio, 1880.
4. *Atlas of Geauga County, Ohio*, H. B. Stranahan & Co., Cleveland, Ohio, 1900.
5. *Burton Independent*, Burton, Ohio, June 26, 1884.
6. *Geauga Leader*, Burton, Ohio, September 5, 1884; October 16, 1907; January 1, 1913; February 21, 1922.

Appendix I

Copy of coal contract signed by Howard Pfouts, Edward Blunt, and David John on May 27, 1884.

Coal Contract.

Edward Blunt
and
David John
WITH
Howard Pfouts

Received for Record
November 11th 1884 at 8 30 o'clock P.M.
Recorded in Book No 152
in Geauga County Records of
Deeds Vol 1 Page 401 & 402
O. A. Wills
Recorder

COAL CONTRACT. REGISTER PRINTING HOUSE, Youngstown, Ohio.

Article of Agreement, Made and entered into this Twenty Seventh day of May A. D. 1884, by and between Howard Pfouts of Burton Geauga Co Ohio party of the First Part, and Edward Blunt and David John of Hiram Portage Co Ohio party of the Second Part,

Witnesseth, That in consideration of One Dollar received, and of the covenants and agreements of the SECOND PARTY, to be performed as hereinafter stipulated, the said party of the FIRST PART does hereby Bargain, Sell and Convey unto the said SECOND PARTY all the ~~MINERAL STONE~~ COAL that may underlie the following described tract or lot of Land situate in the Township of Burton County of Geauga and State of Ohio and is bounded and described as follows:

On the North by Land of Orlin Foster On the East by Land of John Murphy On the South by Land of Boring Heirs On the West by Land of O. B. Ford and Containing Eighty Acres of Land More or Less

And also grants the exclusive right to test, open, mine and remove said Coal and further grants the right to construct railroads, underground entries, and all necessary buildings and fixtures to facilitate the mining and removing of said Coal.

And it is agreed by the party of the SECOND PART that they will within 18 Months ~~from the date of this Contract, test said land by drilling or otherwise~~ and in case there should be discovered a minable vein or bank of ~~Stone~~ Coal of sufficient quantity and quality to justify the opening and mining of said Coal in the opinion of the said SECOND PARTY, then they agree to mine out said Coal and pay the following rate per ton for all Coal mined on said premises, to-wit: Ten Cents for each ton of 2240 pounds of merchantable Coal, Payments to be made and continue in the following manner, to-wit: To make payment ~~semi-annually~~ for all the Coal mined from said land, that is to say, a settlement to be had on the first of January and July of each year as ~~nearly as practicable~~, and payment to be made in full for ~~all Stone and~~ Royalty due up to each date, respectively, and after One and a half years from the date of this Contract, said SECOND PARTY agrees to mine out and remove annually One Hundred Tons of said Coal to the ~~ton or pay for that amount as it should~~

It is Further Agreed, By the parties hereto that the sum of ~~Fifty~~ Dollars advanced by said SECOND PARTY to the FIRST PART, and ~~Fifty~~ Dollars of Coal, is, and shall be considered as advance royalty to be deducted from the royalty of the first excess of Coal mined over

It is also Agreed, That all Coal mined shall be weighed and the weight to be kept in a book, which shall be open to the inspection of the said FIRST PARTY and it is further agreed between the parties that the SECOND PART is to have the privilege of using the said railroads and ~~buildings~~ fixtures for the purpose of mining and removing Coal from other lands ~~of~~ and ~~stone~~ buildings ~~and fixtures~~ by paying to the party of the FIRST PART the sum of Twenty five Dollars per year as long as they use them for transporting Coal

It is Further Agreed, That said party of the SECOND PART shall have the right to abandon this Contract at any time they shall determine that said Coal is in quantity, quality or condition no longer minable with economy and profit, and remove their machinery and other structures and property from said land

And we the parties by the signing and sealing of this Contract, bind ourselves, our heirs, our assignees and legal representatives to strictly adhere to the several covenants and agreements of this Contract, as witness our hands and seals the day and year above written

Signed, Sealed and Delivered in Presence of
Howard Pfouts [SEAL]
Edward Blunt [SEAL]
David + John [SEAL]
mark [SEAL]
[SEAL]

State of Ohio
County of Geauga
Township of Burton

On this 27th day of May A. D. 1884, before me a Notary Public in and for said County personally came all of the parties above named, who severally acknowledged the signing, sealing and execution of the foregoing instrument to be their voluntary act and deed for the uses and purposes therein mentioned; that they are ~~not~~ interested in and desire that the same may be recorded as such.

W. S. Metcalfe Notary Public

Know all Men by these Presents, That Edward Blunt and David John of Mineral Ridge in the County of Trumbull and State of Ohio party of the SECOND PART in the within contract described made by Howard Pfouts to ~~me~~ on the Twenty Seventh day of May A. D. 1884, do hereby assign, transfer and set over the said contract, unto D. E. Owens of Geauga County Ohio with all the property and rights of property interests covers and possessions of every kind therein conveyed to ~~me~~; To Have and to Hold to them their assignees aforesaid and to their legal successors in said property and rights forever.

In Witness Whereof, We have hereunto set our hands and seals, this Second day of May 1891

Signed, Sealed and Delivered in Presence of
Geo. H. Stuart
E. E. Owens
Edward Blunt [SEAL]
David + John [SEAL]
mark

STATE OF O.
Trumbull
On this 27th day of May 91
appeared the said Edward Blunt & David
acknowledged that they did sign and seal the foregoing instrument, and acknowledged the same to be their free act and deed.

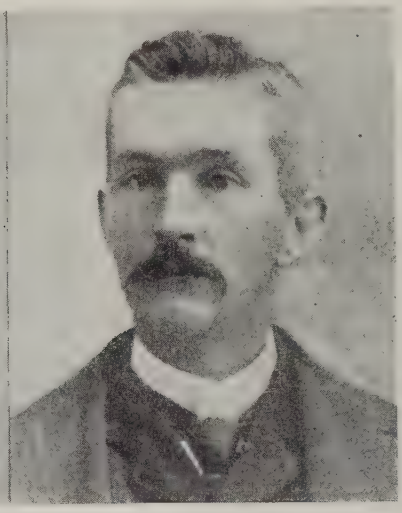
Harold L. Stuart, N.P.

Appendix II

BIOGRAPHIC SKETCHES

A. David Elsworth Owen
1847–1922

David Elsworth Owen was born in Wales on July 6, 1847. His parents emigrated to the United States the following year and settled at Mineral Ridge in Trumbull County, Ohio. He was reared in that town and by diligent effort was able to attend Iron City Commercial College in Pittsburgh. After his graduation he became an accountant and followed that profession during much of his life. About 1880 he became interested in the coal deposit near Burton, Ohio, through his father-in-law and others and eventually secured the mining rights and operated mines at North Burton. Although mining began in 1884, Mr. Owen and his family did not move from Mineral Ridge to North Burton until 1886. From that year until 1900 he engaged in mining, farming and storekeeping. In 1900 Mr. Owen moved his family to Burton Village where he pursued varied activities. He was postmaster from 1905 to 1913. A short time after his retirement from that office his health failed. His death occurred on February 8, 1922. He was the father of ten children, four sons and two daughters of whom survived him. He was a member of the Disciple Church and the Masonic Lodge.



B. Howard Pfouts
1857–1907

Howard Pfouts was born in Wayne County, Ohio, on October 27, 1857. When he was seven years old his parents moved to Beach City, Ohio, where he resided until shortly after his marriage to Miss Clara Walter in 1881. The same year he moved to the farm at North Burton which is now the home of his son, Zeil. He was a farmer throughout his life and lived on this farm until his death in October, 1907. His relatively early death was caused by an accidental fall from a tree. His farm was the site of Ohio's northernmost coal mine, and all of the mining operations were carried on during his lifetime. He was the father of four children, all of whom survived him. He belonged to the Grange and to the Methodist Church and at the time of his death was a member of the Board of Education.

OVIPOSITOR STUDIES OF THE LEAFHOPPER GENUS ERYTHRONEURA

(Homoptera: Cicadellidae)

MARY AUTEN TRAUTMAN,
Franz Theodore Stone Laboratory,
The Ohio State University,
Put-in-Bay, Ohio

Since determination of species in *Erythroneura* is based mainly on wing venation, color pattern, and inner male genitalia, it was believed that a study of ovipositors might lead to discovery of characters that would be of use in identification of females. Such a study was begun in 1937. Most of the work was done at the Stone Laboratory, the remainder at Ashland College. I wish to express my appreciation to Dr. D. M. DeLong for his early assistance in the work; to Dr. F. H. Frison for loan of material from the Illinois Natural History collections; to Mrs. Dorothy J. Knull for identification of specimens, for use of material, and advice; and to Dr. T. H. Langlois, the present Director of the Stone Laboratory, for use of facilities. I also wish to express my appreciation to Ashland College for giving me the opportunity to continue these studies while teaching there.

METHOD OF PREPARATION OF OVIPOSITORS

The tip of the abdomen of a mounted specimen was removed by the use of minuten nadeln. This was soaked in 70% alcohol, using artists' porcelain paint dishes for this purpose. One hour was sufficient for softening, although a longer period of time was not detrimental. The ovipositor sheath and valvulae were then dissected under binoculars with minuten nadeln and dehydrated on the slide by first removing as much of the alcohol as possible with a small piece of cheese cloth. The ovipositor was then shifted to a dry place on the slide after which a drop of dioxane was added and immediately removed with the aid of cheese cloth. Next a drop of thin balsam was placed on the genitalia and a cover glass put in place. The following step was the most delicate of the whole process. The cover slip was gently but firmly rotated in such a manner as to slip the four ovipositor blades apart. This was accomplished with the aid of a heavy, No. 7, insect pin. The position of the heavy-toothed blade was marked with india ink and the slide, after drying for several days, was ready for study. No staining was necessary since the amber color of the chitin gave satisfactory outline of the ovipositor.

INTRA-SPECIFIC COMPARISONS OF OVIPOSITORS

Erythroneura basilaris (Say), *E. compta* McA. and its variety *E. compta* var. *rufomaculata* McA., and *E. tricincta* Fitch were chosen for studies of large series to determine whether there are variations within the species. These were selected because they form well marked series, and individuals of each species were collected from the same host on the same day, indicating that they should belong to identical species. *E. basilaris* (Say) was collected on July 5, 1938, from red elm (*Ulmus fulva*) on North Bass Island, Ohio. *E. compta* McA. on July 22, 1937, from cultivated grapes (*Vitis* sp. and *Muscadinia* sp.) on North Bass Island, Ohio, and *E. tricincta* Fitch on July 19, 1938, from cultivated grapes on Middle Bass Island, Ohio.

Ovipositor slides of 53 specimens of *E. basilaris* (Say), 95 specimens of *E. compta* McA. and 89 of *E. tricincta* Fitch were prepared. After making camera

TABLE I

SHOWING CONFORMITY OF OVIPOSITOR FORM IN SPECIES OF FIVE GROUPS OF *Erythroneura*.

COMES GROUP

	TYPICAL	ATYPICAL		TYPICAL	ATYPICAL
aclys McA.	3		*elegans* McA.	6	
nudata McA.	2		*infuscata* (Gill.)	4	
beameri Rob.	9		*kanwakae* Rob.	9	2
bistrata	9		*ontari* Rob.	10	
cancellata McA.	3		*pontifex* McA.	7	
coloradensis (Gill.)	11		*rubra* (Gill.)	5	
comes (Say)	31	5	*tricincta* Fitch.	9	1
compta McA.	15		*vitifex* Fitch.	4	4
corni Rob.	5		*vitis* (Harris)	14	4
delicata McA.	9	1	*vitis* var. *corona* McA.	13	

MACULATA GROUP

abjecta Beamer	2		*era* McA.	6	
accola McA.	4		*gemina* McA.	3	
adunca Beamer	3		*hartii* (Gill.)	4	
affinis Fitch.	14		*hymac* Rob.	2	1
arta Beamer.	10		*illinoiensis* (Gill.)	6	1
basilaris (Say)	15		*ingrata* Beamer.	3	
bella McA.	6		*kansana* Baker	4	3, 1, 1
bigemina McA.	2	1	*knighti* Beamer	6	4, 1
brevipes Beamer	4		*lawsoni* Rob.	11	1, 1
calamitosa Beamer	1	1, 1, 1	*lata* Beamer.	2	
campora Rob.	7	6, 4, 1	*maculata* (Gill.)	12	2
carmini Beamer	3		*minor* Beamer	3	
certa Beamer.	12	4, 2, 2, 1	*morgani* (DeL.)	12	
concisa Beamer.	2		*omani* Beamer	4	
confirmata McA.	4		*pallida* Knull and Auten.	2	
consueta Beamer	3		*pyra* McA.	8	
contracta Beamer	2	1	*rotunda* Beamer	2	
curvata Beamer.	5		*torella* Rob.	3	
delongi Knull and Auten.	3		*trivittata* Rob.	3	
dira Beamer.	3		*ungulata* Beamer	2	
parallela McA.	5		*usitata* Beamer	5	

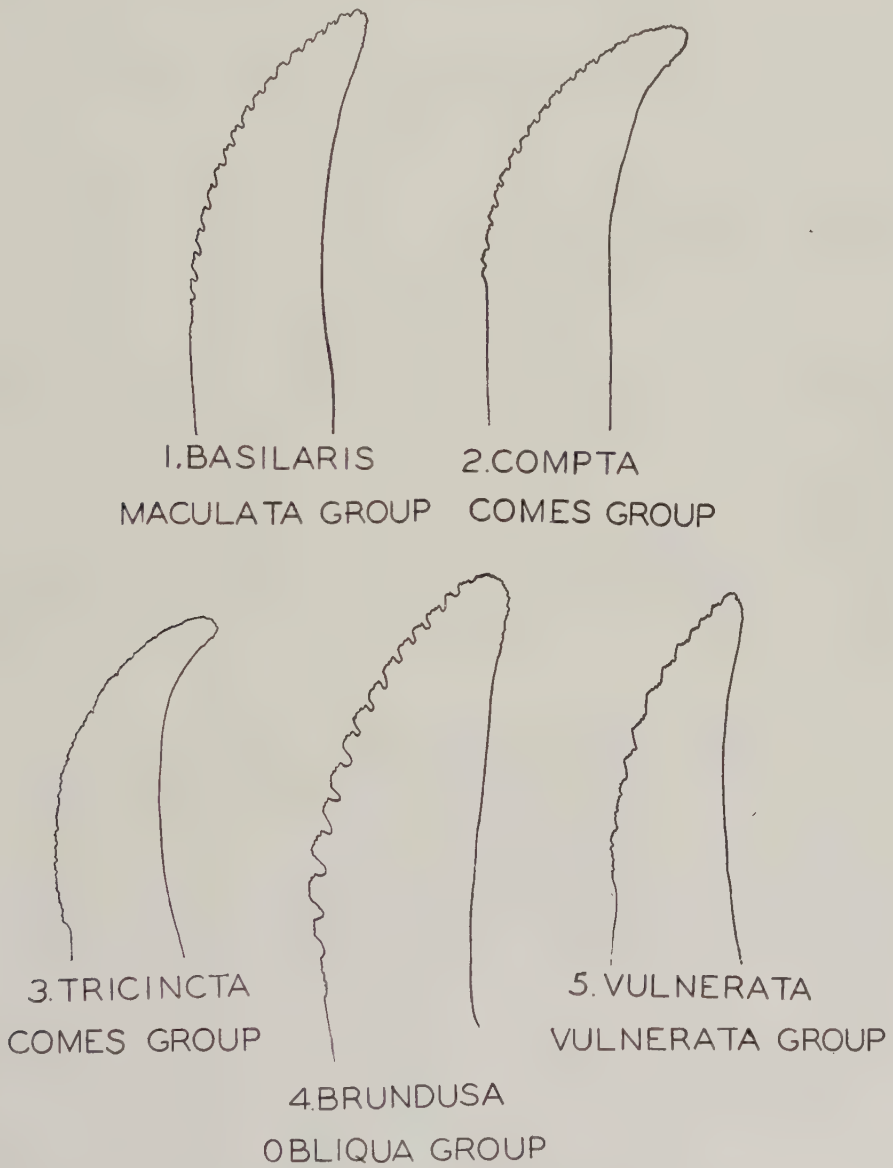
OBLIQUA GROUP

albescens Beamer	6		*funesta* Beamer	6	
angularis Beamer	9	1	*gleditsia* Beamer	3	
apacha Baker	4		*hamata* Beamer	3	
atrimucronata Beamer.	2		*kanza* Rob.	7	
bitincta McA.	2		*lawsoniana* Beamer.	3	
brundusa Rob.	10		*plena* Beamer	7	
clavata DeL.	4	3	*rubens* Beamer	2	
crevecoeuri (Gill.)	2		*rubroscuta* (Gill.)	3	
cruciformis Beamer	4		*tenuispica* Beamer.	5	1
diffisa Beamer.	8	4	*tridens* Beamer	2	
electa McA.	2	1	*stolata* McA.	2	
fulvocephala Rob.	4	4, 2, 2			

VULNERATA GROUP

nigerrima McA.	7		*vulnerata* Fitch.	16	
nigra (Gill.)	3		var. *fulmina* McA.	2	

lucida drawings of a sample of each species the other slides were compared with these drawings by placing the slide on the stage of the microscope and following the outline of the ovipositor by means of the camera lucida. This method of checking eliminated making drawings of all 237 slides.



FIGS. 1–5. Projection drawings of the coarse-toothed median valvulae of the ovipositors of five species of *Erythroneura*.

The coarser-toothed median valvula was used for this study although the lateral valvulae and the finer-toothed median valvula may possess interesting characters. The median valvula was found to be different in each species studied. The general

shape of the blade, length of toothed area, and slant and depth of teeth are apparently specific, although minor variations in number of teeth are present.

E. basilaris (Say) in figure 1 shows heavy dentition, general arrangement of the teeth in two subdenticles, and an angular rather than a curved tip, resulting in the ovipositor having an almost straight dorsal edge. All 53 specimens studied showed these characteristics.

E. compta McA. in figure 2 shows that the teeth are of an irregular low type and the tip of the blade is broad and toothed both dorsally and ventrally. The tip is greatly curved, resulting in a concave dorsal margin. All 95 specimens of *E. compta* McA. and its variety *rufomaculata* McA. conformed to this general pattern.

E. tricincta Fitch in figure 3 shows that the teeth are very fine and merely dent the edge of the blade, a constant character. The tip is curved and more pointed than in either *basilaris* or *compta*.

After making studies of the three large series it seemed reasonable to include two smaller series representing the obliqua and vulnerata groups. Ten specimens of *E. brundusa* Rob., a well marked species, were used and all conform to the general pattern illustrated in figure 4. Figure 4 shows coarse teeth, somewhat as in *E. basilaris* (Say) although deeper and not divided into two subdenticles. The dorsal margin is slightly sinuous. Sixteen specimens of *E. vulnerata* Fitch showed the general pattern illustrated in figure 5. In this figure the toothed margin is somewhat of a staircase type, slightly flattened, and with the subdenticles on the riser.

In recapitulation, the characters shown by these drawings, namely, the coarse teeth of two subdenticles in the maculata group, the distinctive curved tip and fine, irregular teeth in the comes group, the very coarse teeth and sinuous dorsal margin in the oblique group, and the staircase angle of the teeth together with the pointed tip extending slightly ventrad in the vulnerata group, are sufficiently definite to be used with color pattern and wing venation to place individuals in their proper group.

INTER-SPECIFIC COMPARISONS OF OVIPOSITORS

The ovipositors of other species of *Erythroneura*, previously identified on the basis of wing venation, color pattern, and association with males, were studied. The results are given in Table I. Number of specimens studied are indicated by the numbers in the columns under the headings "Typical" and "Atypical." A specimen was considered typical if its combination of characters agreed with the characters of the majority of the specimens referred to as that species. Atypical specimens were those which varied from this combination of characters. These variants probably belong to other species and are the result of inability to identify the females with only the aid of wing venation, color pattern, and association of males. As many as four types of variants (species?) were recorded under a species.

From the evidence presented I conclude that the coarser-toothed median valvula of the ovipositor is of sufficient constancy within a species to be of use in identification.

In this paper no attempt was made (1) to make a key for species identification, (2) to describe the detailed characteristics for any species, (3) to describe the variations present within a species, (4) or to describe the variations occurring within a group. That considerable specific differences occur within groups is demonstrated in the compta group, figures 2 and 3, where differences in size and shape of teeth between *compta* and *tricincta* are very evident, yet their group relationship is plainly indicated by marked similarity in the general shape of the median valvula. Obviously the next step is to make keys for species identification, using ovipositor characters together with wing venation and color pattern as is done with the males.

DESCRIPTIONS OF SIX TYPHLOCYBAS FROM THE UNITED STATES

(Homoptera: Cicadellidae)

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The Ohio State University,
Columbus 10, Ohio

Five of these Typhlocybas belong to the Rosae Group and the sixth to the Danae Group. Unless other deposition is indicated all material is in the collection of the writer.

Typhlocyba cassiopeia n. sp.

Robust, cream colored, eyes pale, vertex and pronotum yellow-tinged, scutellum white, elytra yellow semihyaline, apical cells faintly clouded, creamy white below. This species is near *T. pomaria* McAtee.

Female genital segment three times as long as preceding, only slightly produced, rounded, ovipositor black-tipped, exceeding pygofer. A pair of black spots half way from base separated by width of ovipositor. Inner male genitalia: In ventral view aedeagus shaft narrowed on outer third, lateral processes almost parallel and in front of shaft, diverging gradually, sinuate on outer half, a third longer than shaft; in lateral view, aedeagus small, curved dorsad a third of distance from base at right angles to it, shaft slender, inconspicuous, lying dorsad between a pair of heavy lateral processes which exceed it by a third; ninth segment with ventral angle subrectangular, slightly pigmented, dorsal margin rounded obtusely; outer claspers rather stout, narrowed after middle to spoon-shaped pigmented apices which diverge a little; inner claspers slender, outcurved, aciculate.

Length: Male and female, 3½ mm.

Male holotype, allotype and paratypes, Colorado Springs, Colo., July 19, 1938, D. J. & J. N. Knull, collectors; paratypes, Vineland Station, Ontario, W. L. Putman, collector, taken on a series of dates between July 27 and August 2, from 1938 to 1941, reared from *Prunus serotina* Ehrh. Paratypes in the Canadian National Collection, No. 5503.

Typhlocyba putmani n. sp.

Yellowish white, more yellow on vertex, golden yellow below; eyes tan; elytra shining subhyaline. Related to *T. pomaria* McAtee, but spine of pygofer not as prominently falcate.

Last ventral segment in female with margin faintly sinuate, slightly emarginate over ovipositor which is black-tipped and exceeds pygofer by its width. Male genitalia: In lateral view pygofer spine protruding slightly from ventral posterior corner, sharp, heavy, dark, lying along posterior margin of pygofer, aedeagus with processes evenly curved and tapered from base to pointed apices which are directed latero-caudad, shaft hidden by a process to apex which protrudes ventrally at about one-third length of process; from ventral view, aedeagus three-pronged, shaft tapering to a fine point, a pair of lateral processes, each about a fourth longer than shaft, separated from shaft at base by about twice its width, extends roughly parallel to its entire length, becomes sinuate and turns latero-caudad at apex. Styles of usual type.

Length: Male, 4 mm.; female, 4½ mm.

Male holotype, allotype and paratypes, Vineland Station, Ontario, July 16, 1940, W. L. Putman, collector, from *Cornus* spp.; other paratypes with same data collected July 12 and 13, 1940. Types in Canadian National Collection, No. 5504; paratypes retained by author.

Named for W. L. Putman, who has done interesting work in rearing leafhoppers.

Typhlocyba oneka n. sp.

Slender, pale yellowish white, elytra semihyaline, below cream-colored, eyes pale.

Female, last ventral segment large, concave, roundly, almost semicircularly produced on outer half, no indentation, a pair of dark points one-third distance from apex separated by more than width of ovipositor, sometimes indistinct; ovipositor exceeding pygofer by more than its width. Male genitalia: Ninth segment with posterior angle produced dorsad forming less than a right angle, margin rounded, ventral angle a little sinuate, darkened at tip, sharp, almost a right angle. Outer claspers long and slender, tapered gradually, constricted on outer third which is spatulate and curved laterad, pigmented toward apex; inner clasper hairy at base, outcurved, slender, somewhat aciculate. Aedeagus from lateral view slender, bifid at apical fifth, curved at a right angle with base about one-fourth distance from base; a pair of very delicate slender processes arises just ventrad to base, extends two-thirds length of shaft, the parts diverging slightly toward apices.

Length: Male and female, 3½ mm.

Male holotype, allotype and paratypes, Cranberry Lake, N. Y., July 15, 1920, from *Corylus*, Osborn & Drake, collectors. Types in the Herbert Osborn Collection at The Ohio State University.

Typhlocyba shawneeana n. sp.

Slender, creamy white with translucent elytra and inner male genitalia remarkably different from any known species.

Male genitalia: Ninth segment almost square on outer margin, ventral corner pigmented; outer plates of moderate length, tapering gently to diverging apices which are swollen knob-like and pigmented; inner claspers rather heavy, enlarged blade-like before aciculate, divergent apices; aedeagus in lateral view complex, composed of a pair of heavy ventral processes arising, swollen at base and curving gently to apex; and a heavy shaft, not quite as long as processes, bifid at apex and with a pair of lateral arms projecting laterad before point of separation of apical arms, exceeding them in length, apical arms divergent; in ventral view shaft is very broad.

Length: Male, 3½ mm.

Male holotype and paratypes, Shawnee Forest, Scioto Co., Ohio, June 9, 1943; paratypes, Monroe Co., Ohio, July 6, 1943; and paratype, Hocking Co., Ohio, September 19, 1943; all collected by D. J. & J. N. Knull.

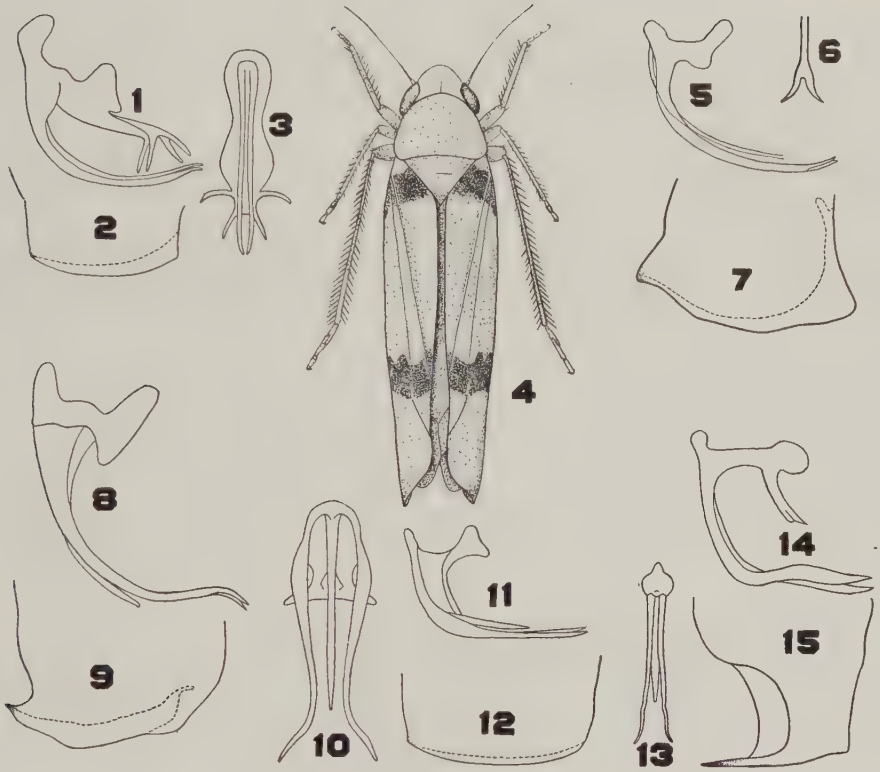
Typhlocyba hockingensis n. sp.

Small, shining golden yellow above and below, gray eyes, elytra semihyaline, apical cells faintly smoky. Distinguished from all but *T. pomaria* McAtee by the falcate process from posterior border of size of ninth segment which is heavily chitinized, pigmented; distinguished from *T. pomaria* McAtee by heavier lateral processes of aedeagus.

Female, last ventral segment long, produced on median third, ovipositor exceeding pygofer by more than its width. Male, spine of pygofer pigmented, strongly protruding from ventral corner; aedeagus in lateral view with weak, short shaft, near apex of connective which is about as long as shaft between it and heavy pair of ventral processes which is three times as long as shaft, extends straight down on upper half, then curved abruptly dorsad at a little more than a right angle and is enlarged on apical half, then narrowed gradually to pointed apex; from ventral view shaft is not visible, processes are about parallel entire length, sinuate, apices turned in.

Length: Male and female, 3¼ mm.

Male holotype, Hocking Co., Ohio, June 19, 1943; allotype, May 29, 1938; paratypes, May 29, 1938, to September 16, 1943; also paratypes as follows: Shawnee Forest, Scioto Co., Ohio, June 9, 1943; Great Smoky Mt. Nat. Park, Tenn., June 21, 1942; all collected by D. J. & J. N. Knull; and Indian Gap, Smoky Mts., Tenn., September 3, 1939, Mary Auten, collector. Paratypes in Collection of The Ohio State University and in the Canadian National Collection, No. 5505.



EXPLANATION OF PLATE

1. Lateral view of aedeagus of *T. shawneeana* n. sp.
2. Lateral view of hind margin of ninth segment, *T. shawneeana* n. sp.
3. Ventral view of aedeagus, *T. shawneeana* n. sp.
4. Dorsal aspect of *T. hinei* n. sp.
5. Lateral view of aedeagus of *T. oneka* n. sp.
6. Ventral view of apex of aedeagus shaft, *T. oneka* n. sp.
7. Lateral view of hind margin of ninth segment, *T. oneka* n. sp.
8. Lateral view of aedeagus, *T. putmani* n. sp.
9. Lateral view of hind margin of ninth segment, *T. putmani* n. sp.
10. Ventral view of aedeagus, *T. putmani* n. sp.
11. Lateral view of aedeagus, *T. cassiopeia* n. sp.
12. Lateral view of margin of ninth segment, *T. cassiopeia* n. sp.
13. Ventral view of aedeagus, *T. cassiopeia* n. sp.
14. Lateral view of aedeagus, *T. hockingensis* n. sp.
15. Lateral view of margin of ninth segment, *T. hockingensis* n. sp.

Typhlocyba hinei n. sp.

Near *T. bifasciata* Boh., an European species, but with scutellum pale. Chalky white with dark brown eyes and two transverse bands on the elytra, the anterior extending from sides of scutellum across clavus, extending slightly caudad on corium, reaching costal margin but leaving pale anterior humeral part; the posterior band before crossveins, extending from apex of clavus curving a little cephalad toward costal margin, and narrowed. The elytra seem opaque but for costal area between bands and apical cells which are fumose semihyaline, veins white. Below white. This species belongs to the Danae Group.

Length: Female, 4 mm.

This beautiful insect is named for the late J. S. Hine, who collected a specimen. It occurs on white oak along with *T. tunicarubra* Gill.

Described from a series of females. Holotype and paratypes, Delaware Co., Ohio, July 8, 1942; paratypes July 1 and 15, 1943; all collected by D. J. & J. N. Knull; and a paratype, Wauseon, Ohio, July 8, 1896, J. S. Hine, collector. The Hine paratype is in the Herbert Osborn Collection at The Ohio State University.

NOMENCLATORIAL NOTES ON CICADELLIDAE

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Columbus, Ohio

The following new names are proposed for one genus and four species with names already preoccupied:

Genus

Calanana n. n. for *Calana* DeLong (Ohio Jour. Sci., 36: 218, 1936), not *Calana* Gray, Proc. Zool. Soc. London, 15: 148, 1847 (Mollusca).

Species

Nesosteles neglecta var. *pallidens* n. n. for *Nesosteles neglecta* var. *pallida* (DeLong & Davidson) (Ohio Jour. Sc. 33:55, 1933), not *Nesosteles pallidus* (Osborn) (Anns. Ent. Soc. Amer. 19: 352, 1926).

Dikraneura lentana n. n. for *D. lenta* DeLong (Ohio Jour. Sci. 38: 218, 1938), not *D. lenta* McAtee, Jour. N. Y. Ent. Soc. 34: 160, 1926.

Empoasca davidsoni n. n. for *Empoasca mucronata* Davidson & DeLong (Ohio Jour. Sci. 38:90, 1938), not *E. mucronata* Ribaut, Bull. Soc. Hist. Nat. Toulouse 65: 150, 161, 1933.

Typhlocyba pruniella n. n. for *Typhlocyba pruni* DeLong & Davidson (Ohio Jour. Sci. 34: 16, 1934), not *T. pruni* Edwards, Entomologists Monthly Magazine 25:158, 1888.

A SYSTEMATIC STUDY OF THE MAIN ARTERIES IN THE REGION OF THE HEART—AVES IX.

Coliiformes—Part 1[1]

FRED H. GLENNY[2]
1148 Linden Avenue, Akron 10, Ohio

In several recent studies on birds, the writer has been able to present the significant basic ordinal and important family arrangement-patterns of the main arteries in the neck and thoracic regions. The present paper deals with the arrangement of these arteries in the Coliiformes.

It is significant that, although only three species of Colies are represented in this study, Sclater (1924) recognizes but one genus and six species for the order. The Colies are, therefore, an extremely small group of birds which are found exclusively in Africa.

The taxonomic position of this order of birds has been a subject of much interest. At one time they were placed among the passerine Fringillidae, and later were grouped in the older order Coraciiformes. Wetmore (1940), however, gives them ordinal rank, which, based upon several anatomical evidences, is entirely justifiable.

The information thus far presented in this and previous papers may subsequently afford some clue to possible avian phyletic and genetic relationships, and may later come to be used, in part, as an aid in taxonomic treatises.

MATERIALS[3]

Single specimens of the Speckled Mousebird *Colius striatus* Gmelin (No. 227154), the Red-faced Mousebird *Colius indicus* Latham (No. 290394), and the Blue-naped Mousebird *Colius macrourus* (Linné) (No. 290606) were dissected and diagrams of the main cervical and thoracic arteries prepared.

The materials for this study were from the collection of alcoholic specimens of the United States National Museum.

OBSERVATIONS

The arrangement-pattern of the arteries of the neck and thorax is the same for each of the three species of Colies represented in this study.

The innominate arteries (2) arise from the aortic root (1) and pass anteriorly and diagonally toward the base of the neck where they divide to form the common carotid artery and the subclavian artery. The latter gives rise to the coracoid major artery (15), which arises from the ventral face of the subclavian artery between the common carotid and axillary arteries, the intercostal artery (14), which arises from the posterior face of the subclavian just behind the coracoid major, the axillary artery (12), which arises from the anterior face of the subclavian between the common carotid and the anterior pectoral arteries, and finally the two pectoral arteries (13) in order. The coracoid minor artery (11) arises from the axillary artery. The subclavian arteries and branches present a bilaterally symmetrical arrangement.

The common carotid derivatives are not bilaterally symmetrical in their arrangement and must, therefore, be treated separately.

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[1]Contribution from the Department of Zoology, University of Toronto, Toronto, Ontario, Canada.

[2]Formerly Assistant, Department of Zoology, Univ. of Toronto. Now on Active Service with the Army of the United States.

[3]Numbers after the species are the U. S. National Museum catalogue numbers of specimens used for this study.

The right common carotid (10) gives rise to the right ductus shawi (16) which sends off branches to the trachea (19), syrinx (18), bronchi, and oesophagus; the superficial cervical artery (29), which sends off a scapular artery (24) and other branches to the cervical lymph glands and musculature; a vertebral artery (27); and a secondary or accessory ascending-oesophageal artery (26) from the base of which a short basi-oesophageal artery (28) frequently springs.

The left common carotid artery sends off a tracheo-oesophageal artery (17) from which springs the left ductus shawi (16) which sends off branches to the same organs and other structures as does the right vessel; the cervico-vertebral artery (21) divides into the vertebral (22) and superficial cervical (23) arteries (the latter sends off a scapular artery (24) to the left shoulder region); and the internal carotid (trunk) artery (25) which enters the hypapophysial canal and passes anteriorly to the head where it sends off branches to the left and right sides of the head. Each of these vessels then divides into the complimentary internal and external carotid branches (Glenny, 1943).

The ligamentum aortae (7) is present in each of the three species and is attached anteriorly to the left pulmonary artery (6). The ligamentum botalli (8) is present as a small vestige, but is much reduced and tends to fuse distally with the right radix aortae (4). In *Colius indicus*, at least, the right ligamentum botalli maintains a thread-like proximal attachment to the right pulmonary artery.

DISCUSSION

It should be pointed out that the Coliiformes are laevo-carotidinae as are the Trogoniformes (Glenny, 1943), certain Coraciiformes (Meropidae, Upupidae, and Phoeniculidae) (Glenny, 1943), the Piciformes (Glenny, 1943) and the Passeriformes (Glenny, 1942). In arrangement-pattern, these forms closely resemble one another, and differ in only minor respects.

Lowe (1939) points out that except for certain minor structural differences the Swifts and Humming-Birds closely resemble the Perching Birds which he would place in a subordinal position in the larger order Passeriformes. At the same time he would place the Pici, Eurylaimi, Cypseli and Trochili as other suborders in the Passeriformes. He also suggests that perhaps some of the Coraciiformes (Wetmore, 1940) might likewise be placed in this larger order.

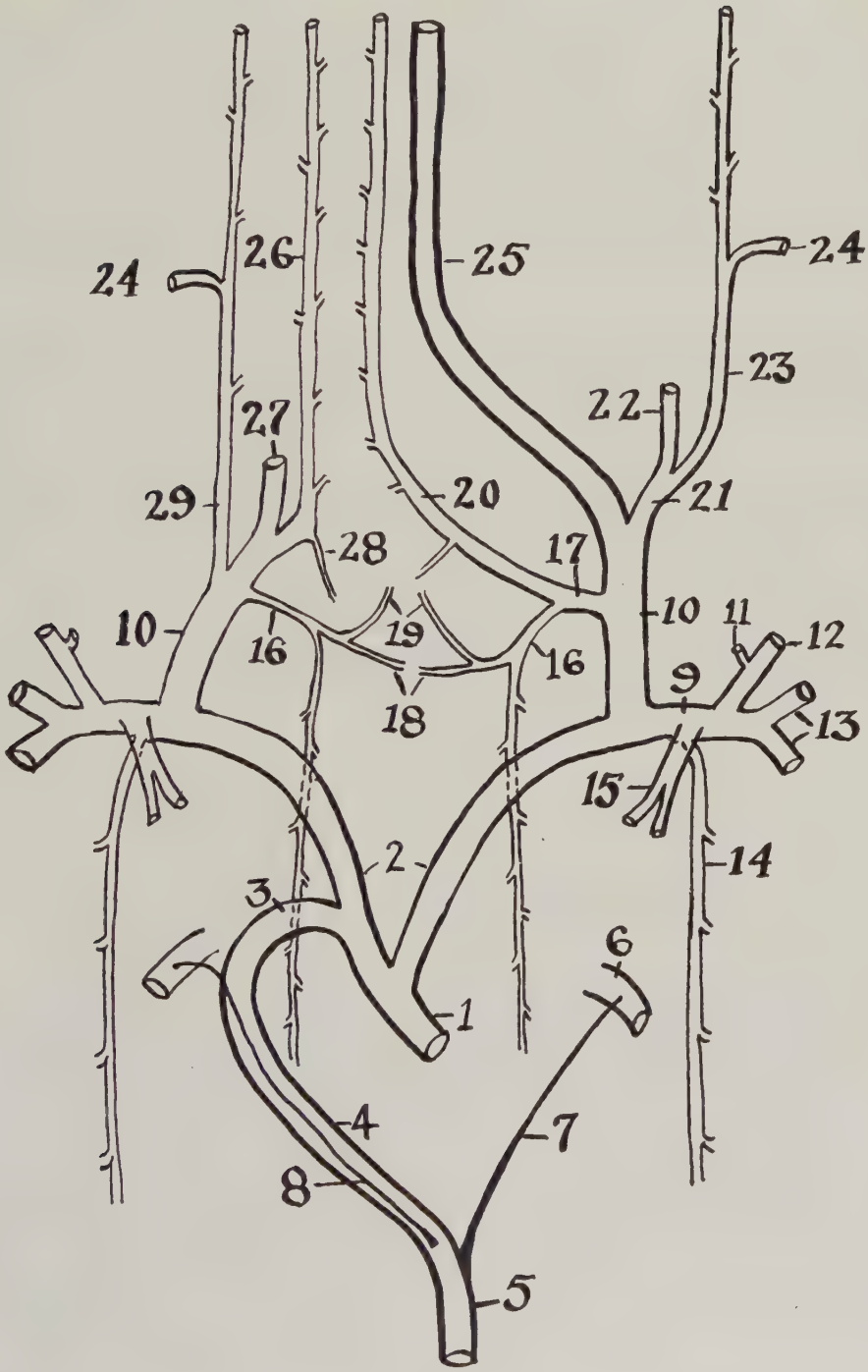
Based upon my own studies, I am inclined to agree with Lowe, if we are to try to establish probable relationships of larger orders of birds, rather than accord ordinal rank to all groups which do not have all of the important characteristics of extant forms.

EXPLANATION OF PLATE

Figure 1. Diagrammatic representation of the main arteries in the neck and thorax of *Colius striatus* Gmelin. Ventral view.

KEY TO ABBREVIATIONS

1. Aortic root.
2. Innominate arteries.
3. Systemic (4th aortic) arch.
4. Right radix aortae.
5. Dorsal aorta.
6. Pulmonary artery.
7. Left ligamentum aortae.
8. Right ligamentum botalli.
9. Subclavian artery.
10. Common carotid artery.
11. Coracoid minor artery.
12. Axillary artery.
13. Pectoral arteries.
14. Intercostal artery.
15. Coracoid major artery.
16. Ductus shawii.
17. Tracheo-oesophageal artery.
18. Syrinx artery.
19. Tracheal artery.
20. Primary ascending-oesophageal artery.
21. Cervico-vertebral artery.
22. Left vertebral artery.
23. Left superficial cervical artery.
24. Scapular artery.
25. Internal carotid (trunk) artery.
26. Secondary or accessory ascending-oesophageal artery (right internal carotid *trunk* artery).
27. Right vertebral artery.
28. Basi-cervical artery.
29. Right superficial cervical artery.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While it may be thought by some that there is great variation in soft structures such as arteries, and therefore, these structures cannot be used satisfactorily as evidences of trends in evolution, my experience in this work cannot substantiate such claims. In fact, by a thorough study of the arterial system in the neck and thorax, from early embryonic stages through to the mature adult, one can grasp the main and significant trends of development. This is likewise true of the development-patterns of other structures such as the bony or skeletal system, and of the musculature. Although virtually nothing with reference to growth curves (of bones, etc.) in birds has been done, such work as has been carried out recently would seem to confirm our concept of ordinal developmental-patterns. Such findings are necessary to aid in the final establishment of ordinal and family relationships.

If we are to accept a poly-reptilian concept of avian evolution, we must regard the origin of such birds as the Rhea, Ostrich, Emu, and Cassowary as different from that of the Tinamous, Galliformes, and Anseriformes, and at the same time we should postulate a different origin for the Penguins. In the same vein, we may further conceive of the other birds as being divided into at least two or more groups, present-day forms of which probably had somewhat different reptilo-avian ancestors. Of this latter group, the present-day representatives of the Coliiformes, Trogoniformes, certain Coraciiformes, Piciformes, and Passeriformes[4] along with Cypseli and Trochili[5] may have sprung from a common stock since all of these show distinctive characteristics (several of which are held in common). Individual lines of evolution and development have taken place so that ultimately they have assumed their own distinctive characteristics which are the reasons for according them ordinal rank by our present taxonomists.

It is, therefore, my opinion that if the present orders of birds are to be reclassified, based upon natural relationships, in an effort to establish primitive relationships, the above general group should be presented as the last main order.

ACKNOWLEDGMENTS

The writer wishes to express his gratitude to Dr. Alexander Wetmore, Assistant Secretary, Smithsonian Institution, and Dr. Herbert Friedmann, Curator of Birds, United States National Museum, for their helpfulness and cooperation in making available these and other materials for study, and to Dr. E. Horne Craigie, Department of Zoology, University of Toronto, and Dr. A. L. Rand, Curator of Birds, National Museum of Canada, for their suggestions and criticisms during the progress of these studies and in the preparation of this paper.

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THREE NEW ZYGNEMATACEAE FROM ARKANSAS

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During a study of the algae collected in the Boston Mountain region of Arkansas, two new species of *Zygnema* and one of *Spirogyra* were found. Following are the descriptions of these species.

Zygnema insignisporum sp. nov.

Vegetative cells 24–28μ x 39–71μ, conjugation scalariform, receptive gametangia inflated on the conjugation side; zygospores globose to ovoid 32–35μ x 32–35μ, outer wall of two colorless layers of which the outermost is smooth, the inner scrobiculate with pits 4–5μ in diameter and about 7μ apart; median wall punctate, yellow.

Zygnema transeauianum sp. nov.

Vegetative cells 30–32μ x 20–60μ; conjugation scalariform, receptive gametangia enlarged or slightly inflated on the conjugating side; zygospores globose to ovoid 25–35μ x 33–40μ, somewhat compressed; median spore wall yellow-brown reticulate with large irregular pits 7–12μ across.

Spirogyra castanacea sp. nov.

Vegetative cells 34–37μ x 100–173μ, with plane and walls; 2 to 3 chromatophores making 2 to 3 turns in the cell; conjugation scalariform, tubes formed by both gametangia; receptive cell inflated on both sides; zygospores mostly broadly ellipsoid, rarely ovoid, 48–52μ x 69–73μ, median spore wall chestnut brown, strongly reticulate.

A general summary of the algae of the Boston Mountain region was published in Abstracts of Doctoral Dissertations (No. 38) by the Ohio State University Press, 1942.

SYMPOSIUM ON PREMEDICAL EDUCATION

Alpha Epsilon Delta, national honorary premedical fraternity, sponsored a symposium on Premedical Education at the Cleveland meeting of the Association for the Advancement of Science in September, 1944. More than seventy teachers and administrators from various colleges throughout the country attended. Dr. H. E. Setterfield, national president of Alpha Epsilon Delta, opened the Symposium and Dr. Victor Johnson, secretary of the Council on Medical Education and Hospitals of the American Medical Association, presented a paper on the "Objectives in Premedical Education" from the medical point of view. Dr. C. I. Reed of the department of physiology at the University of Illinois was to have presented a paper summarizing some opinions on premedical training as determined among the faculty and students of the five medical colleges in Chicago. Unfortunately, Dr. Reed was unavoidably absent.

A spirited discussion followed the formal remarks and showed the realization of the many important problems involved in premedical training. Plans for further investigation of these problems were proposed by Dr. Setterfield. Among these is the publication of the papers presented on the Symposium in the November issue of *The Scalpel* of Alpha Epsilon Delta which will be distributed to a large number of teachers and administrators along with a list of the more important questions for discussion brought out at the Symposium. The remarks and suggestions submitted will be published in pamphlet form and circulated among premedical teachers and others interested.

Copies of these publications may be had upon request to Dr. Maurice L. Moore, Secretary of Alpha Epsilon Delta, 3853 Lakewood, Detroit 15, Michigan.

REVIEW PAPERS

(Papers appearing in this section are invited reviews of subjects of wide current interest.)

PENICILLIN: A POTENT NEW CHEMOTHERAPEUTIC AGENT

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HISTORY

In 1929 Dr Alexander Fleming (1) at St. Mary's Hospital in London observed a clear zone around a mold contaminant on petri dishes inoculated with *Staphylococcus aureus*. This phenomenon stimulated him to isolate and culture the mold on broth to see if the mold would produce a substance inhibitory to the growth of bacteria under these circumstances. His hypothesis proved to be correct; for, whenever he placed a drop or two of the broth on which the mold had grown on plates on which *Staphylococcus aureus* or each of several other bacteria were growing, large clear areas occurred after a short time as the drops diffused through the agar.

Dr. Fleming found by various methods that several different strains of staphylococci were inhibited by the broth with little variation among strains. Other pathogenic organisms which proved to be quite susceptible were *Streptococcus pyogenes*, pneumococci, gonococci, meningococci, *Corynebacterium diphtheriae*, and some strains of *Streptococcus viridans*.

Many organisms were entirely unaffected by the broth. Among these were *Escherichia coli*, *Eberthella typhosa*, *Pseudomonas pyocyaneus*, *Proteus vulgaris*, *Vibrio comma*, *Friedlander's bacillus*, *Hemophilus influenzae* and Flexner's dysentery bacillus.

Dr. Fleming found the broth containing the inhibitory substance for certain bacteria to be no more toxic or irritating than the broth itself, when injected into animals. In the summary to this original paper he modestly proposed that the antibacterial substance might find clinical application in infections caused by organisms susceptible to it.

Since the mold which elaborated the antibacterial substance was recognized by Dr. Fleming to be a member of a large genus of molds, *Penicillium*, he named the substance penicillin. Although the word has been pronounced several ways and there has been much discussion as to the correct one, the majority usage among workers in the field appears to be pen-i-cil′-lin.

Because penicillin was very unstable and was difficult to produce in large quantities, it excited little interest during the next ten years. Fleming reported its use as a selective bacteriostatic agent for purposes of differentiation of bacteria in two or three papers. In 1932, Clutterbuck et al. (2) devised ways to grow the mold in larger amounts and further described the chemistry of the antibiotic substance.

A sudden new interest in penicillin followed the announcement of Florey, et al. (3, 4) that penicillin is very effective therapeutically and is of extremely low toxicity in contrast to the relatively high toxicity of the antibacterial substances, gramicidin and tyrocidine, isolated by Dubos from soil bacteria. Their papers also included new methods of extracting the antibiotic substance from the mold as well as improved methods of purification.

Since the papers of Florey, et al. appeared in 1940 and 1941, reports of several thousands of cases treated with penicillin have appeared in about three hundred papers.

The startling, almost miraculous, therapeutic results reported by Florey and his co-workers in the successful treatment of hopelessly infected individuals excited such wide interest that in 1941 Florey was brought to the United States by the Rockefeller Foundation to attempt to institute larger scale production than was possible in war-torn England. Here he interested the National Research Council and the Northern Regional Laboratory of the Department of Agriculture at Peoria along with several large pharmaceutical concerns in the possibility of large-scale production. At that time his yields were only about two units per ml. which were too small to be commercially practicable when amounts of the order of one million units were apparently necessary to treat deep-seated infections effectively.

The next important advance, which made large-scale production feasible, came with the discovery by Dr. Andrew Moyer at the Northern Regional Laboratory that addition of corn-steep water (a by-product of the corn refining industry) to the medium on which the mold was grown increased the yields of penicillin to better than forty units per ml.

PRODUCTION

At present all penicillin is produced by growing highly selected strains of the mold, *Penicillium notatum* (ordinary untested green bread or cheese mold is entirely unsatisfactory) on a suitable medium from which the penicillin is then extracted.

Probably the foremost problem is the maintenance of sterility. It seems paradoxical that such a potent antibacterial agent as penicillin must be produced by a mold grown under aseptic conditions; but it is well known that organisms which are not susceptible to penicillin, may destroy it very readily. Thus Abraham and Chain (5) extracted a substance from *Escherichia coli* which they named penicillinase since it destroyed penicillin and it had some of the properties of an enzyme.

The optimal culture temperature for penicillin production by the mold appears to be 24° C. The carbon source in the medium is usually lactose; sodium nitrate may be used as the nitrogen source. A host of trace elements has been claimed to be essential for maximum yields by various workers. Among these zinc ions seem to be very important. As stated above, corn-steep water, the composition of which is incompletely known, greatly increases yields.

Three devices are commonly employed to effect aeration (the mold will not grow anaerobically) and the method of culture is named accordingly.

1. Surface culture method. Until several months ago most of the penicillin was produced by this method in commercial installations. Aeration is by simple diffusion and a fundamental requirement is that the medium be not more than two cms. deep for best yields. The essential problem is then one of sterilization, inoculation and maintenance under aseptic conditions for several days of the large surfaces of medium required for commercial production of penicillin. To do this, racks filled with shallow trays are sometimes used but more commonly the flat-type half-gallon milk bottle is used. Some establishments are said to be using several hundred thousands of these. After autoclaving the bottles containing about 400 ml. of medium each, they are inoculated under aseptic conditions with suspensions of the mold spores by means of spray guns. The bottles are piled on their sides so that the maximum surface of medium in the bottle is presented to the mold for growth. After a suitable time (usually 5-7 days) the pH of the medium will have changed from 4 or 5 to about 7, when the contents are dumped into screening devices to separate the mold which is then discarded. The medium filtrate containing the penicillin is then ready for extraction.

2. Submerged Culture Method. Several plants are now using this method which promises to supplant all other methods for commercial production. One establish-

ment uses several tanks which hold thousands of gallons each. Although the yields per ml. are probably somewhat lower than by the surface culture method, the labor requirements are very much less because the filling, sterilization, inoculation and handling of individual bottles is obviated. In this method aeration is accomplished by vigorous bubbling of sterile air through the inoculated medium. The essential problem seems to be one of sterilization of the huge volumes of air required.

3. Bran Method. In this method aeration is brought about by growing the mold on coarse bran wetted with the medium in large trays or in long rotating cylinders.

According to a report given by Coghill (10) the total production of penicillin in this country is increasing rapidly and it was predicted that sufficient would be available to meet the essential needs of both the military and civilian populations before the end of the year. In March, alone, approximately forty billion units were produced by 21 companies; this is greater than the total amount produced in 1943. When all of the plants are producing to capacity it was predicted that at least 200 billion units per month will be produced by the end of 1944.

The present standard is a pure crystalline solid equivalent to 1650 of the old Oxford or Florey units per milligram. Hence the predicted output of the 21 plants will be only about 9 pounds per day.

EXTRACTION AND PURIFICATION

Several methods have been described for the extraction of penicillin from the culture medium on which the mold has grown. Among the simplest of these is that described by Abraham and Chain (7). The pH of the solution containing the penicillin is adjusted to 1.9–2.0 with phosphoric acid when it is immediately shaken with some solvent immiscible with water such as amyl acetate or chloroform. After separation of the phases the aqueous portion is discarded. The amyl acetate containing the penicillin in acid form is then shaken with small portions of water-containing base such as sodium bicarbonate. This reconverts the penicillin to the sodium salt which is selectively soluble in the aqueous phase.

The resulting solution of the sodium salt of penicillin may be purified further by chromatographic adsorption on columns of alumina or other suitable adsorbents. For clinical use further purification is usually unnecessary (although desirable) beyond removal of amyl acetate dissolved in the solution. Usually the solution is filtered through Seitz bacterial filters and then dried by sublimation of the water from the frozen state under reduced pressure. The product is a yellow powder which is quite stable when perfectly dry and especially if kept in the refrigerator For therapeutic use it is then readily dissolved in water or normal saline.

CHEMICAL PROPERTIES OF PENICILLIN

Needless to say there probably never has been a compound whose isolation and determination of structure has stimulated a more intensive and concerted effort by individual chemists and groups of chemists in universities and pharmaceutical houses. Announcement of pure penicillin in the form of its crystalline sodium salt was first made in October, 1943, by McPhillamy and Wintersteiner of the Squibb Institute for Medical Research (6). This was, of course, a most important step forward and an essential one preliminary to chemical scrutiny of the compound. For obvious reasons publication of the structure and synthesis of penicillin is not anticipated for the Duration even though they may be discovered before the War ends.

Because all reports on the chemistry of penicillin which have been published, and notably the splendid work of Abraham and Chain (7), have been of work on impure preparations, only general properties which are unlikely to be affected by the presence of impurities will be summarized here.

In aqueous solution penicillin is most stable in the pH range 5 to 7. Its anti-bacterial properties are destroyed at increasing rates as the pH of the solution is varied increasingly widely from the above stability range. It is this sensitivity to high acidities which results in loss of its activity in contact with gastric juice and makes inefficient its administration by mouth. The higher the temperature of the aqueous solution at a given pH the more rapidly the anti-bacterial properties are lost. Electrometric titration indicates that a lactone ring is opened during inactivation by alkalies.

Penicillin is readily destroyed by hydrogen peroxide and potassium permanganate but is stable to air oxidation.

In the free (acid) form it is readily soluble in fat solvents such as ether, acetone, esters and dioxane. It is less soluble in chloroform and only slightly soluble in benzene and carbon tetrachloride. The free acid dissolved in ether or amyl acetate is stable several days at room temperature; it is inactivated by passing dry hydrogen chloride through the solutions. It is also inactivated by such primary alcohols as methyl, ethyl, benzyl and by ethylene glycol.

The sodium, potassium and ammonium salts are very hygroscopic and hence soon decompose in contact with air. The calcium, strontium, and barium salts are non-hygroscopic relatively stable white powders, especially if kept cold.

Elementary analysis of the barium salt of penicillin obtained by Abraham and Chain with 500 units of activity per milligram corresponded to the formula $C_{24}H_{32}O_{10}N_2Ba$ with a molecular weight of 645; 508 of this is due to the penicillin itself, free from barium.

Meyer, et al. (8) give the formula $C_{14}H_{19}NO_6$ as best fitting their data. Later (9) they succeeded in obtaining the methyl, ethyl, n-butyl and benzohydryl esters by reacting with the corresponding diazo compounds. In vitro the methyl and ethyl esters were quite active, the ethyl more so than the methyl ester. Moreover there was some indication that the stability was increased as evidenced by successful use in treating mice infected with virulent hemolytic streptococci by giving the esters by mouth.

ASSAY

The concentration of penicillin is measured by a bioassay method which depends on its antibiotic properties. Two of the several methods used will be described briefly.

Cup Assay Method.—A susceptible strain of bacteria (usually *Staphylococcus aureus* 209) is cultured on petri dishes on which are evenly distributed five porcelain or glass cylinders so as to form a seal with the inoculated agar. Into two of the cups thus formed is placed a solution of penicillin of known concentration, usually one unit per ml. Into the other three cups is placed the solution whose content of penicillin is to be determined, after having diluted the solution so that its concentration will also be about one unit per ml. The plates are then incubated at 37° C. overnight. In the morning it will be found that wherever the penicillin has diffused through the agar the growth of the cultured bacteria will have been inhibited. There thus results a clear zone of inhibition around each of the cups. A suitable comparison of the average of the diameters of the zones produced by the solution of unknown concentration with the average for the knowns is the basis of the assay. This method is the most widely used because a sterile preparation is unnecessary and because a large number of assays can be made per person per day.

Turbidimetric Method.—Where greater accuracy or greater speed is essential, turbidimetric methods based on the proportionality between penicillin concentration and inhibition of bacterial growth are used. The necessity of using bacterial filters to sterilize the penicillin solutions prior to assay by this method as it is usually employed is its chief draw-back.

Recently a bioassay method was described (29) by the use of which penicillin concentrations may be determined in 60–90 minutes with an error of less than 5%. It depends upon the inhibition of the reduction of nitrate to nitrite by *Staphylococcus aureus* in the presence of penicillin. The nitrite is determined colorimetrically by a modification of the method of Shinn (30).

The Oxford and Florey unit was originally defined as that amount of penicillin which, when dissolved in 50 ml. of meat extract broth, just inhibits completely the growth of the test strain of *Staphylococcus aureus* (11). At the present time penicillin is measured in terms of a pure crystalline standard assigned the value of 1650 units per milligram. From this it is seen that 0.6 gram of crystalline penicillin is equivalent in antibiotic activity to one million units.

ANTIBACTERIAL ACTION OF PENICILLIN

Many lists have appeared showing the susceptibility or insusceptibility of various bacteria and fungi to the action of penicillin in vitro. The one below is that of Hobby, Meyer and Chaffee (12).

Susceptible Strains	Insusceptible Strains
Diplococcus pneumoniae	*Hemophilus influenzae*
Streptococcus hemolyticus	*Escherichia coli*
Neisseria gonorrhoeae	*Eberthella typhosa*
Neisseria meningitidis	*Shigella dysenteriae*
Streptococcus viridans	*Proteus vulgaris*
Bacillus subtilis	*Salmonella paratyphi*
Clostridium welchi	*Salmonella enteritidis*
Clostridium septique	*Pseudomonas aeruginosa*
Clostridium histolyticus	*Pseudomonas fluorescens*
Clostridium sporogenes	*Serratia marcescens*
Clostridium oedemantiens	*Klebsiella pneumoniae*
Clostridium sordellii	*Staphylococcus albus*—1 strain
Lactobacillus	*Micrococcus albus*—1 strain
Cryptococcus hominis	*Monilia albicans*
	Monilia krusei
	Monilia candida

In addition to some of the above organisms, Abraham et al. (4) found the following to be susceptible or insusceptible respectively.

Bacillus anthracis	*Salmonella schottmuelleri*
Corynebacterium diphtheriae	*Salmonella typhimurium*
Clostridium tetani	*Brucella abortus*
Actinomyces bovis	*Brucella melitensis*
	Mycobacterium tuberculosis
	Pasteurella pestis
	Anaerobic streptococci
	Vibrio comma
	Leptospira icterohemorrhagiae

In preliminary animal experiments followed by administration in four cases of early syphilis in men, Mahoney et al. (13) found that penicillin possessed spirocheticidal activity. Susceptibility of the spirochetes which cause relapsing fever (*Borrelia novyi*) was observed by Heilman and Herrell in experimentally infected mice (14).

Evidence is at hand to indicate that penicillin is ineffective in virus infections. Myers and Lenahan (15) observed the development of chicken-pox in a patient under penicillin therapy for osteomyelitis. Robinson (16) found that penicillin was ineffective in protecting mice from the influenza virus PR8.

The foregoing list of organisms which are susceptible to penicillin contains the names of the greatest killers of man. The number of men who have died in all of the wars since the beginning of history is small in comparison to the number who have succumbed to the diseases commonly caused by these organisms. Men-

tion of only a few would strike terror into the hearts of the bravest armies; pneumonia, meningitis, bacteremia, osteomyelitis, empyema, tetanus, gas gangrene, brain abscess, mastoid and middle ear infections, gonorrhea, et cetera.

That penicillin is not a panacea is attested to by the above list of insusceptible organisms. Moreover, recent reports show that there are numerous strains of some of the organisms, which appear in the susceptible list, that are not affected by penicillin. Fisher (17) found 12 insusceptible strains of staphylococci of 102 strains in his *in vitro* studies with crude penicillin. He also encountered several strains of hemolytic streptococci which were not affected by penicillin. Florey (18) reports that Major Scott Thomson found 4 per cent of staphylococci are resistant to penicillin.

The mode of action of penicillin is not clearly understood. Hobby, Meyer and Chaffee (19) found that penicillin usually acts as a bacteriostatic agent but it may not be bactericidal. Actual killing of hemolytic streptococci was not accompanied by lysis. It seemed that penicillin was effective only during active multiplication of the organisms. The rate of killing increased as the penicillin concentration increased within certain limits, when a given number of organisms was present originally; but no penicillin was destroyed or removed from solution in detectable amounts by the organisms. Abraham et al. (4) found no inhibitory effect on the action of penicillin in the presence of pus, blood, serum, tissue autolysates or peptones; this is in contrast to the sulfonamides.

Gardner (20) describes microscopic changes due to a failure of fission in rod-shaped organisms acted upon by penicillin. There occurred a lengthening of the cells due to growth without division and separation of the cells. In the case of *Staphylococcus aureus* Smith and Hay (21) observed an increase in size of the cells which were cultured in broth containing penicillin. As the cells increased in size, imperfect division occurred as evidenced by the appearance of a clear zone across the middle of the cell.

Welshimer (28) found in studies in the Warburg apparatus that dismutation of pyruvic acid by *Staphylococcus aureus* was inhibited by penicillin.

Several studies have appeared concerning the development of a tolerance of susceptible organisms when exposed to penicillin concentrations which would just permit growth. McKee and Houck (23) reported growth of a type III pneumococcus culture, highly virulent to mice, in a thirty-fold increase of penicillin after 55 serial passages in a broth containing penicillin in concentrations that would not completely inhibit growth. Type specificity of these resistant cultures was retained although the colonies grew more slowly and the capsule was smaller. There occurred abnormal forms with a tendency to clump and chain formation. Simultaneously there was a marked decrease in virulence for mice; before passage a lethal dose was about ten organisms but after the fifty-fifth passage, approximately 900 million organisms were required to kill the mice. Nor was the virulence restored after nine mouse passages. Similar treatment with three strains of staphylococci, one strain of *Streptococcus pyogenes* and a type I pneumococcus culture produced the same results. Keefer et al. (24) found that resistance of *Staphylococcus aureus* and other cocci may develop during treatment of patients with insufficient doses of penicillin. However, the penicillin-resistant organisms remained susceptible to the sulfonamides and vice versa.

Penicillin has the widest margin of safety of any known chemotherapeutic agent. Tissue culture studies by Herrell and Heilman (25) showed that the toxicity for lymphocytes, granulocytes, phagocytes and erythrocytes was extremely low with crude preparations containing more than 97 per cent of impurities. Robinson (16), using an impure preparation, found the toxic dose of penicillin to be about 64 times the effective dose when injected subcutaneously into mice. Clinical evidences of toxicity encountered by Keefer et al. (24) such as urticaria, flushing of the face, and local pain at the site of injection were attributable to

impurities which had not been removed. Numerous recent reports in which purer preparations of later and improved manufacture describe no unfavorable clinical reactions whatsoever. In the light of this recent clinical experience with the drug, it seems safe to say that overdosage with pure penicillin is virtually impossible.

ADMINISTRATION

Penicillin has been administered locally as wet dressings, via catheters into wounds and body cavities, in ointments, and as a powder—either as the calcium salt or by insufflation with one per cent penicillin diluted with sulfonamide powder (26). It has also been injected subcutaneously, intramuscularly, intravenously, intraperitoneally, intrathecally and into various body cavities and spaces. In general the present practice is to use it locally for burns, surface infections, wounds, etc.; and intramuscularly at the rate of 5,000-20,000 units every 2–4 hours for systemic administration. Occasionally it is given by continuous intravenous drip in overwhelming infections or where an established bacteremia exists. A distinct disadvantage is that it cannot be given efficiently by mouth because of the rapid destruction of most of it by the acid in the stomach.

FIG. 1, a and b. Front and side views of patient at onset of penicillin therapy. Extensive facial cellulitis and edema of both eyes may be noted; patient moribund; c, appearance of child ninety-six hours later.

The striking effectiveness of penicillin in overwhelming infections susceptible to it is well demonstrated in the case of a patient treated by Herrell (22). Fig. 1 (a and b) are front and side views of the patient at the start of penicillin treatment.[1] According to her father, this four-year-old girl had bitten the inside of her left cheek prior to the appearance of swelling and redness of the left jaw six days before the pictures were taken. On admission, her temperature was 104° F. and breathing and swallowing were difficult. Examination revealed necrosis in the left alveolar lingual region; this was drained by means of a stab wound into which was introduced a small rubber drain. Blood culture was strongly positive for hemolytic *Staphylococcus aureus*. The leukocyte count was 4500 with 37% neutrophils, 62% lymphocytes and 1% monocytes. During the next five days she was given between 20,000 and 30,000 units of penicillin daily intra-

[1]Reprinted from "Further observations on the clinical use of penicillin," by W. E. Herrell, M. D., M.S., Proceeding of the Staff Meetings of the Mayo Clinic, 18: 65-76, 1943, through the courtesy of the author and the Mayo Clinic.

venously. Thirty-six hours after the penicillin was started, the blood became sterile. At the time X-ray revealed pneumonia of the right upper lobe, presumably staphylococcal in origin. Fig. 1 (c) was taken 96 hours after initiation of the treatment, at which time she could again swallow and breathe with little difficulty. Fig. 2 (a) shows the child on the ninth day of treatment when her temperature had become normal. Fig 2 (b and c) show her on dismissal, completely recovered. During the twelve days of treatment the patient had received a total of 196,000 units of penicillin or only 0.12 gram of the drug on the basis of the pure crystalline salt!

OTHER ANTIBIOTICS

As Professor Fleming has remarked, it would be a most unusual accident if the first successful antibiotic would prove to be the best one. At present there is a wide-spread search for other antibiotics which will be effective against pathogenic organisms that are insusceptible to penicillin; or that will be more easily produced, more stable, can be taken by mouth, or that can be readily synthesized. Among the many which have been described are: gramicidin, tyrocidine, streptothricin, streptomycin, actinomycin, clavacin, gliotoxin, penatin, etc., etc. However,

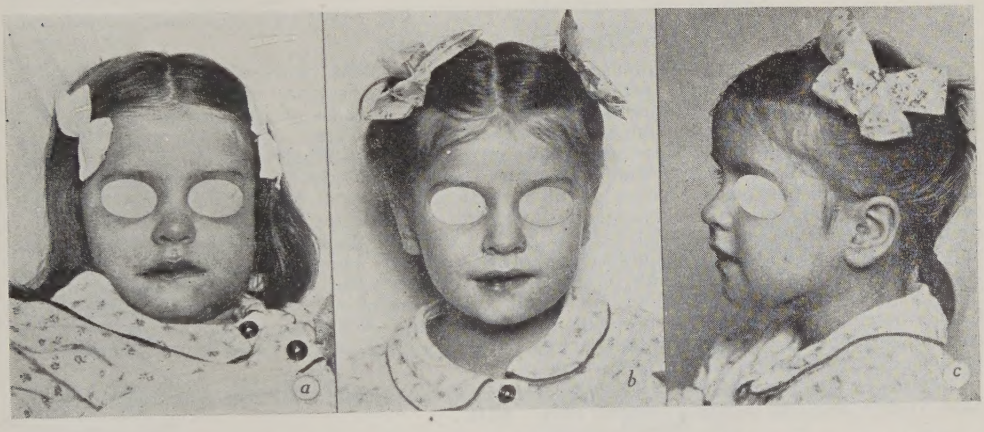

FIG. 2, a. Appearance of patient nine days after onset of treatment; b and c, respectively, front and side views of patient before dismissal. Complete recovery.

most of them do not combine the lack of toxicity with the effectiveness possessed by penicillin. Of particular interest is streptothricin (27) since it is reported to be effective against the organisms that are responsible for typhoid fever and bacillary dysentery, an important group of gram-negative pathogens against which penicillin is entirely ineffective.

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The Problem of Mitosis

Franz Schrader has added another to the list of excellent monographs in the Columbia Biological Series. This volume treats of the problems of mitosis, many of which are as yet quite unexplained. The term mitosis is used in the old inclusive sense of any nuclear division that involves a spindle apparatus and division of chromosomes, and as such includes "meiotic mitosis." The book opens with a careful account of structures involved in the mitotic process, including the spindle apparatus, the kinetochore, the aster and the spindle constituents. Then follows a clear dispassionate account of the various hypotheses of mitosis, including those concerned with pulling, pushing, viscosity and hydration, electrostatics, diffusion, streaming, hydrodynamic forces and tactoids. Related problems of the interphase, the pairing of chromosomes and kinetochores, the nuclear membrane and other subsidiary phenomena make up a challenging chapter. Such conclusions as can be objectively and critically reached are presented in the final chapter. Students of cytology must read this masterful summary before proceeding with further attempts at solving the problems of cell division. A bibliography of nearly 500 titles completes the book. The illustrations are few but very clear, and are used just where they are needed.—*L. H. Snyder.*

Mitosis: The Movements of Chromosomes in Cell Division, by Franz Schrader. 110 pp. New York, Columbia University Press, 1944. $2.00.

Permeability Up To Date

For nearly twenty years there have been no attempts at a monographic treatment of the topic of permeability. Within the past two years two such books have been published. One of these, written by two well-known American authorities on the subject (Brooks and Brooks, The Permeability of Living Cells. Julius Springer, Berlin, 1942), has unfortunately not become available because of transportation restrictions resulting from the war. The other book is "The Permeability of Natural Membranes," by Hugh Davson and J. F. Danielli. This is a volume which will appeal more to specialists than to the general reader, but no one whose work lies within the field of permeability or related phenomena can afford to overlook it. All phases of the topic are discussed and the book should be profitable reading for both plant and animal physiologists. Mathematical formulations of diffusion, rates of penetration, and related phenomena are developed in some detail. There is a graphic chapter on the structure of the plasma membrane. Permeability to various classes of substances such as non-electrolytes, gases, water, proteins, lipoids, ions, weak electrolytes, and dyes are considered as separate topics. One chapter is devoted to the effects of narcotics, another to the effects of temperature on permeability. There are also chapters on such specialized topics as potential measurements and permeability, haemolysis, permeability in relation to secretion and the permeability problems of the kidney. The final chapter is a discussion of the theories of cell permeability. A list of key references is appended to each chapter. There are numerous figures and an index.—*B. S. Meyer.*

The Permeability of Natural Membranes, by Hugh Davson and J. F. Danielli. 361 pp. Cambridge: at the University Press; New York: The Macmillan Co. 1943. $4.75.

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